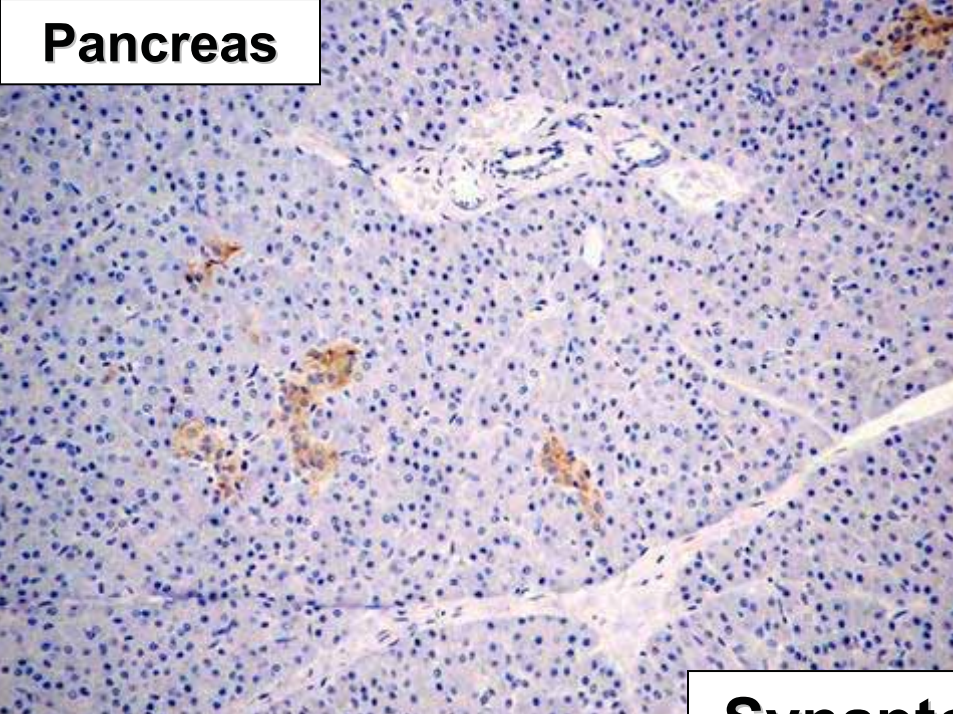


Synapthophysin

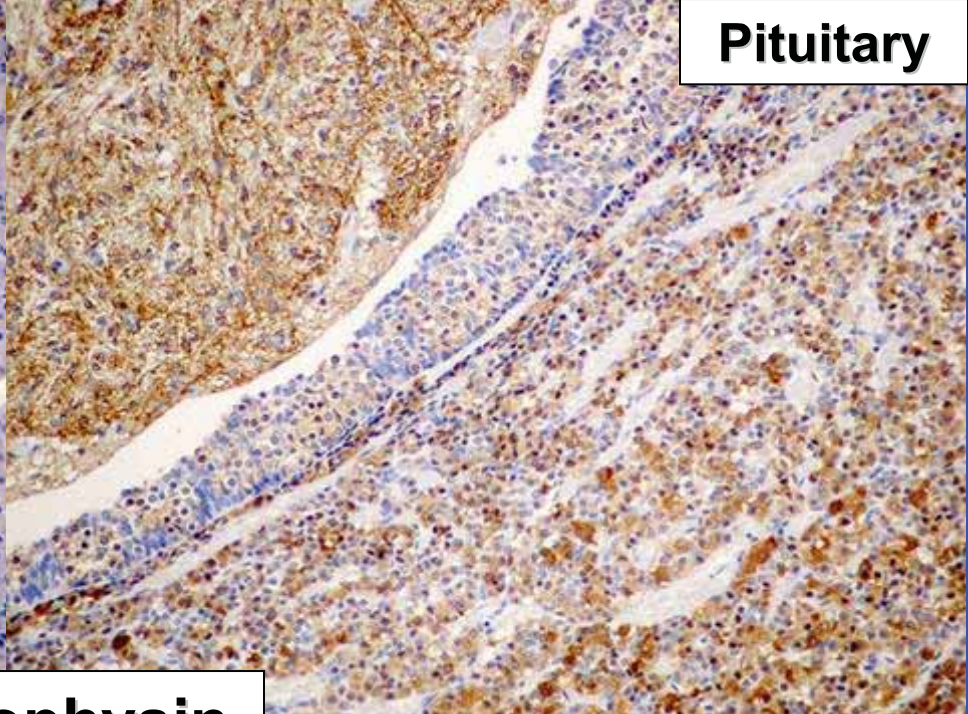


- Calcium-binding 38 kD glycoprotein that is the most abundant integral membrane protein constituent of synaptic vesicles of neurons
- **Also present in neuroendocrine cells**
- Staining pattern:
 - **punctuate - neurons**
 - **diffuse cytoplasmic - neuroendocrine cells**
- Staining for chromogranins and synaptophysin differs between various neuroendocrine neoplasms
- Antibodies should be used complementary
- **Synaptic vesicle protein 2: similar, but rarely used**

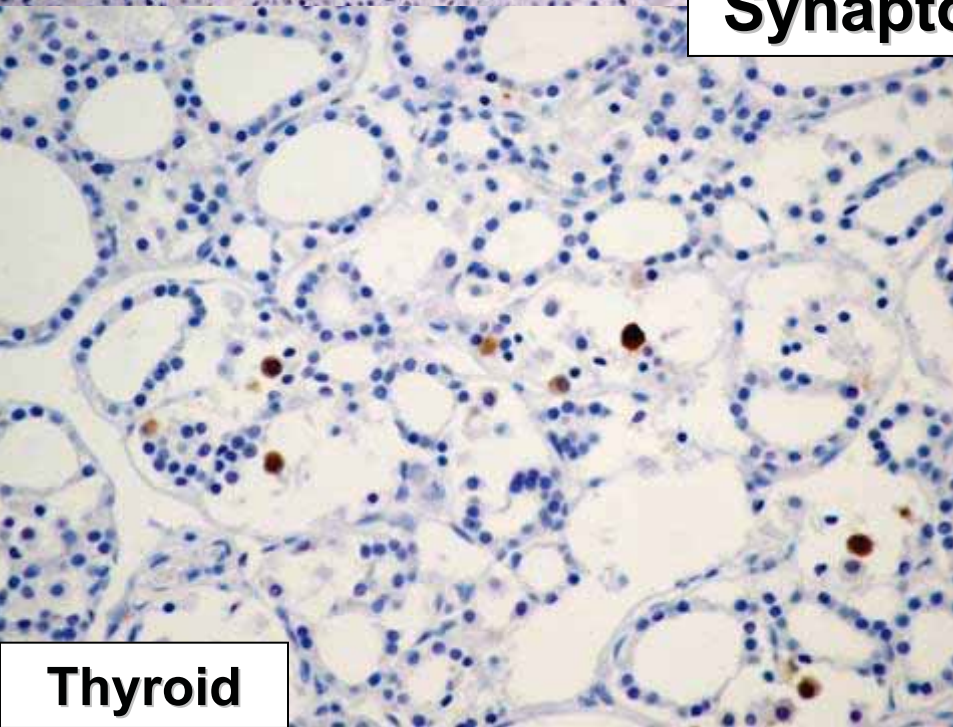
Pancreas



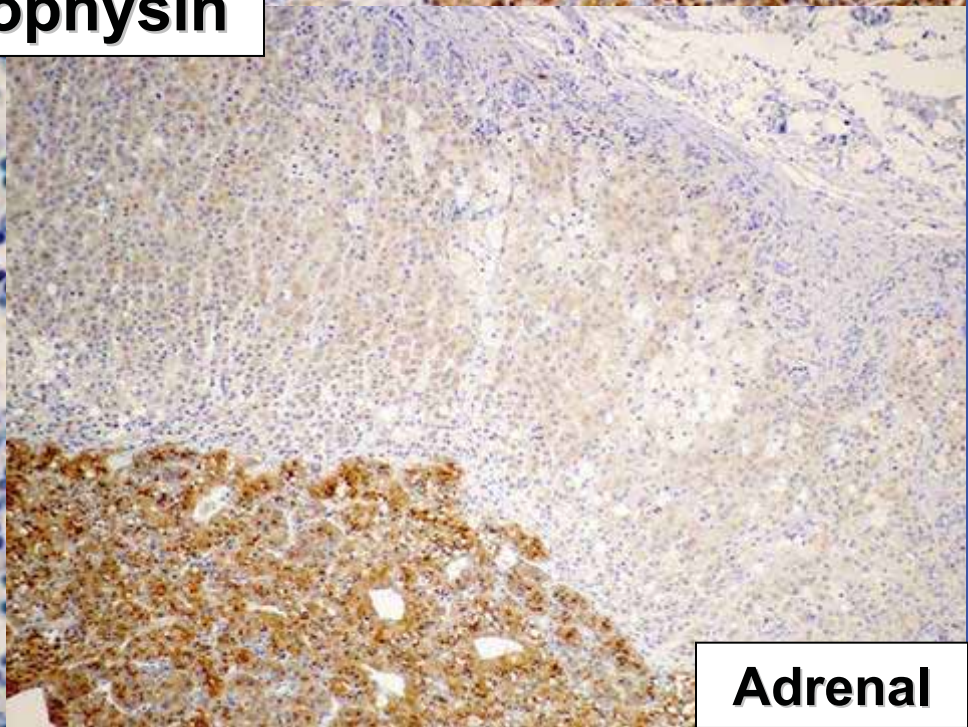
Pituitary



Synaptophysin

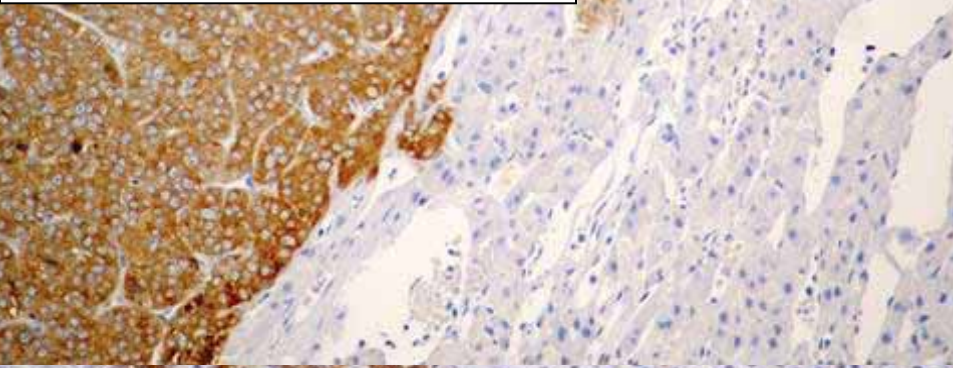


Thyroid

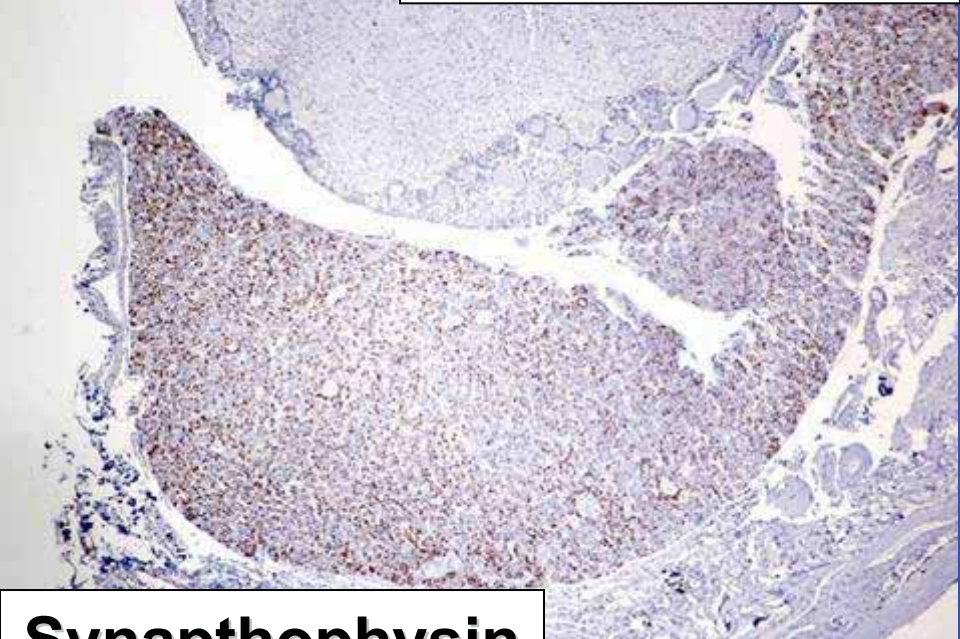


Adrenal

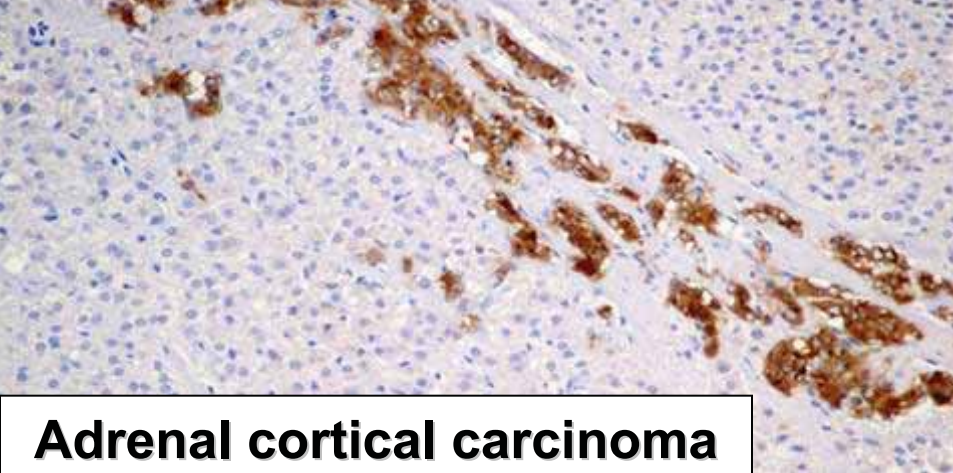
Pheochromocytoma



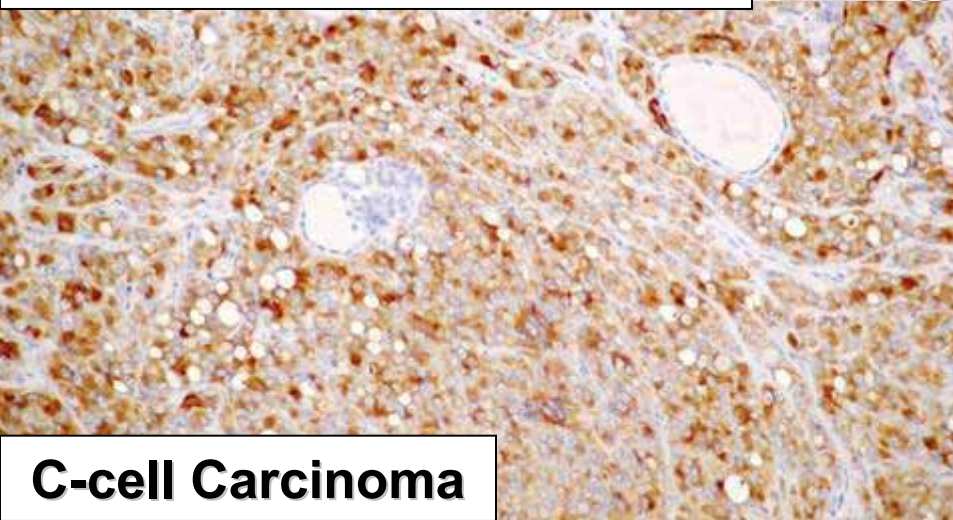
Pituitary Adenoma



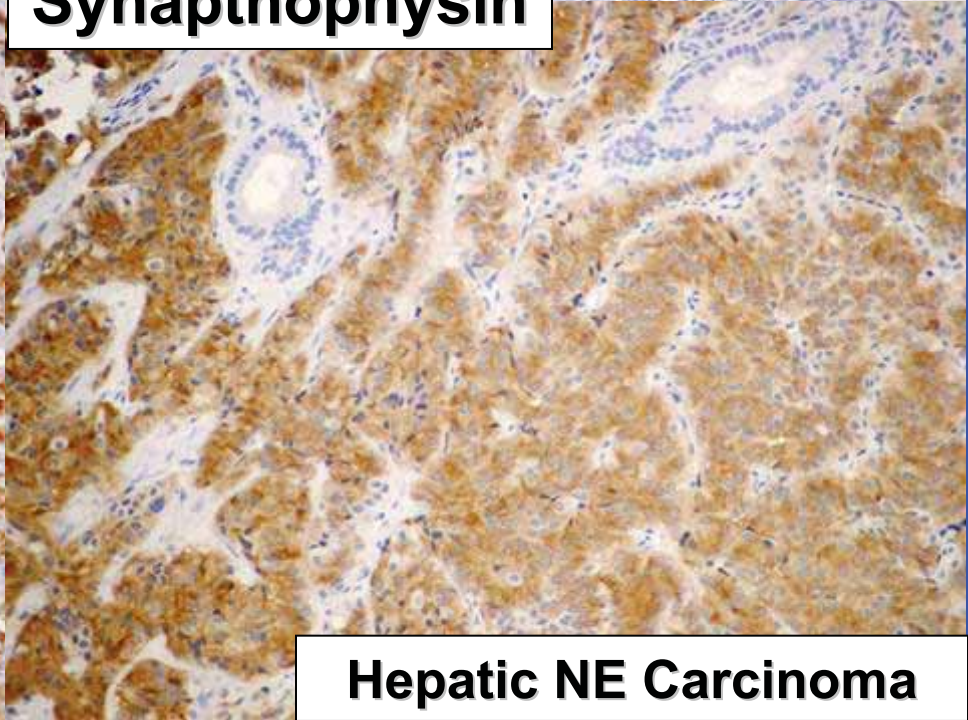
Synapthophysin



Adrenal cortical carcinoma

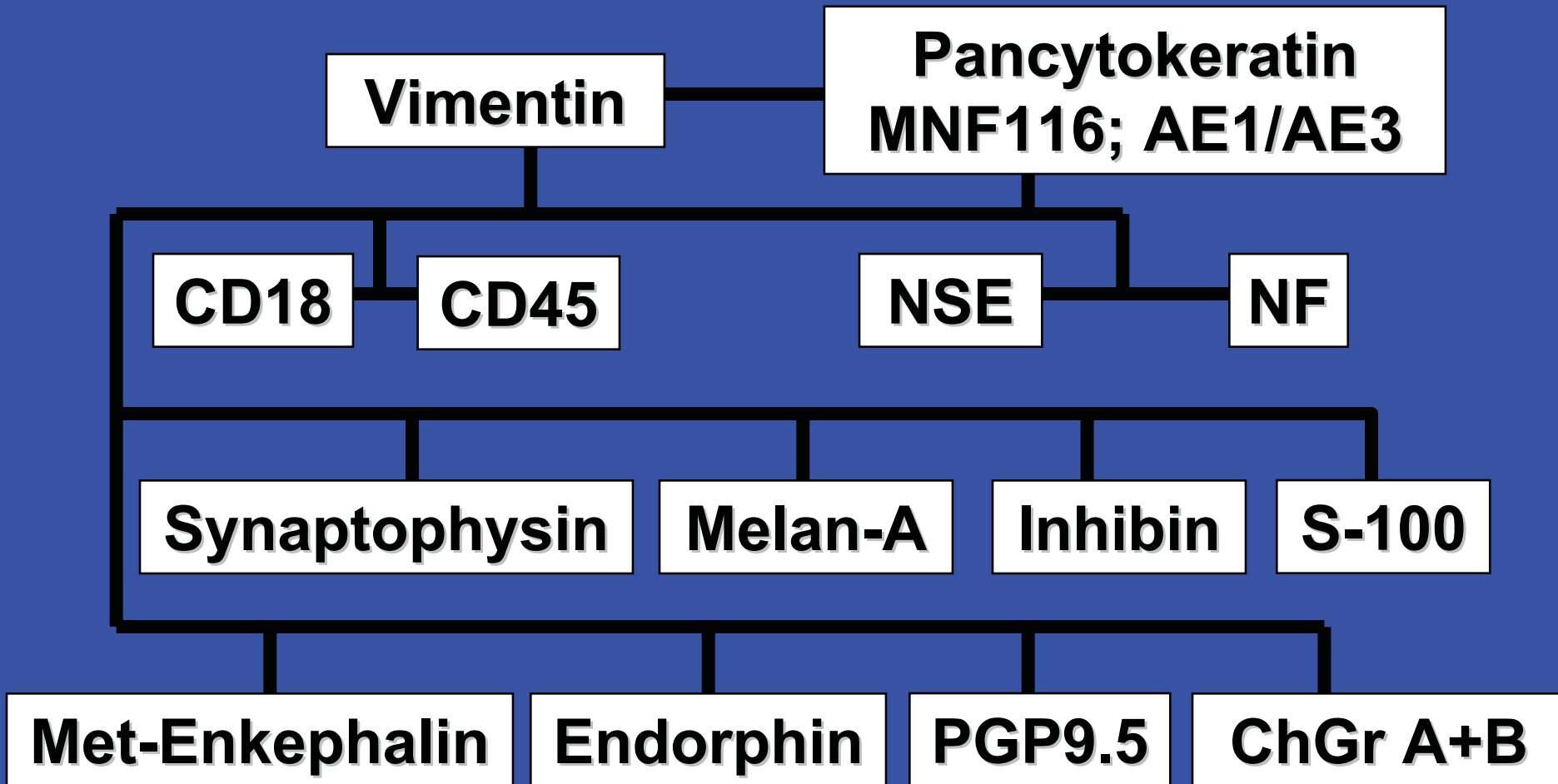


C-cell Carcinoma

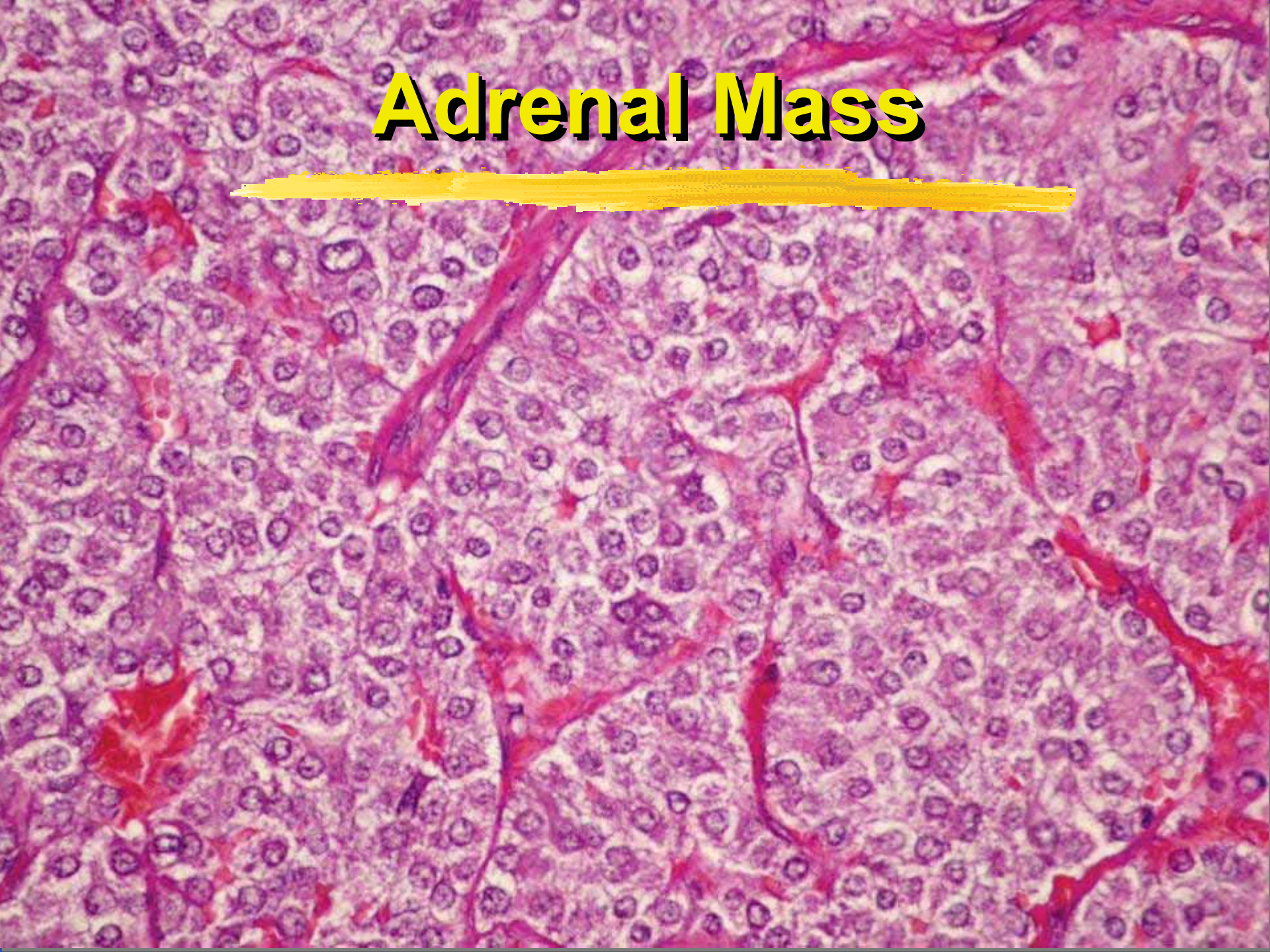


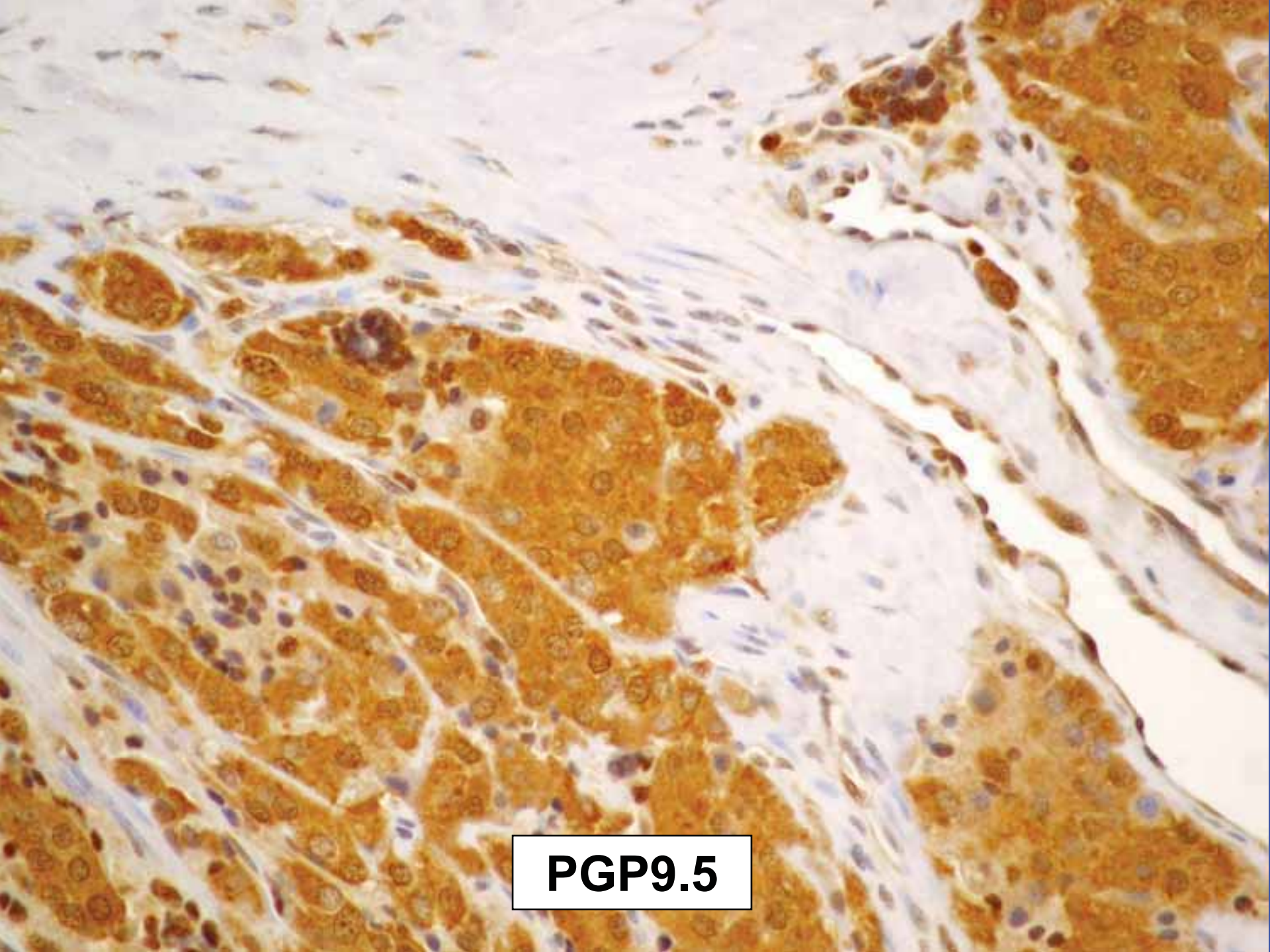
Hepatic NE Carcinoma

Tumors of the Adrenal

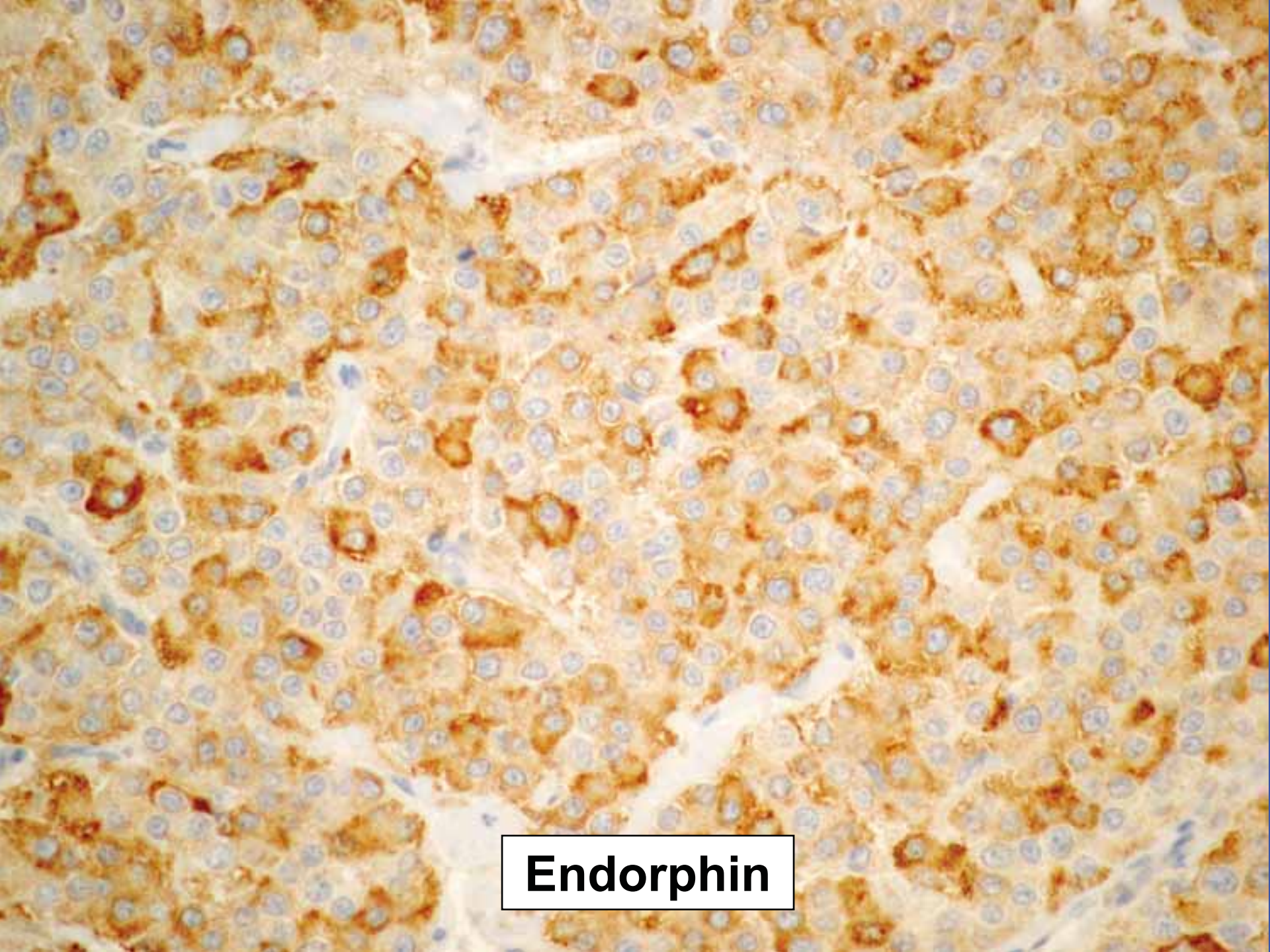


Adrenal Mass

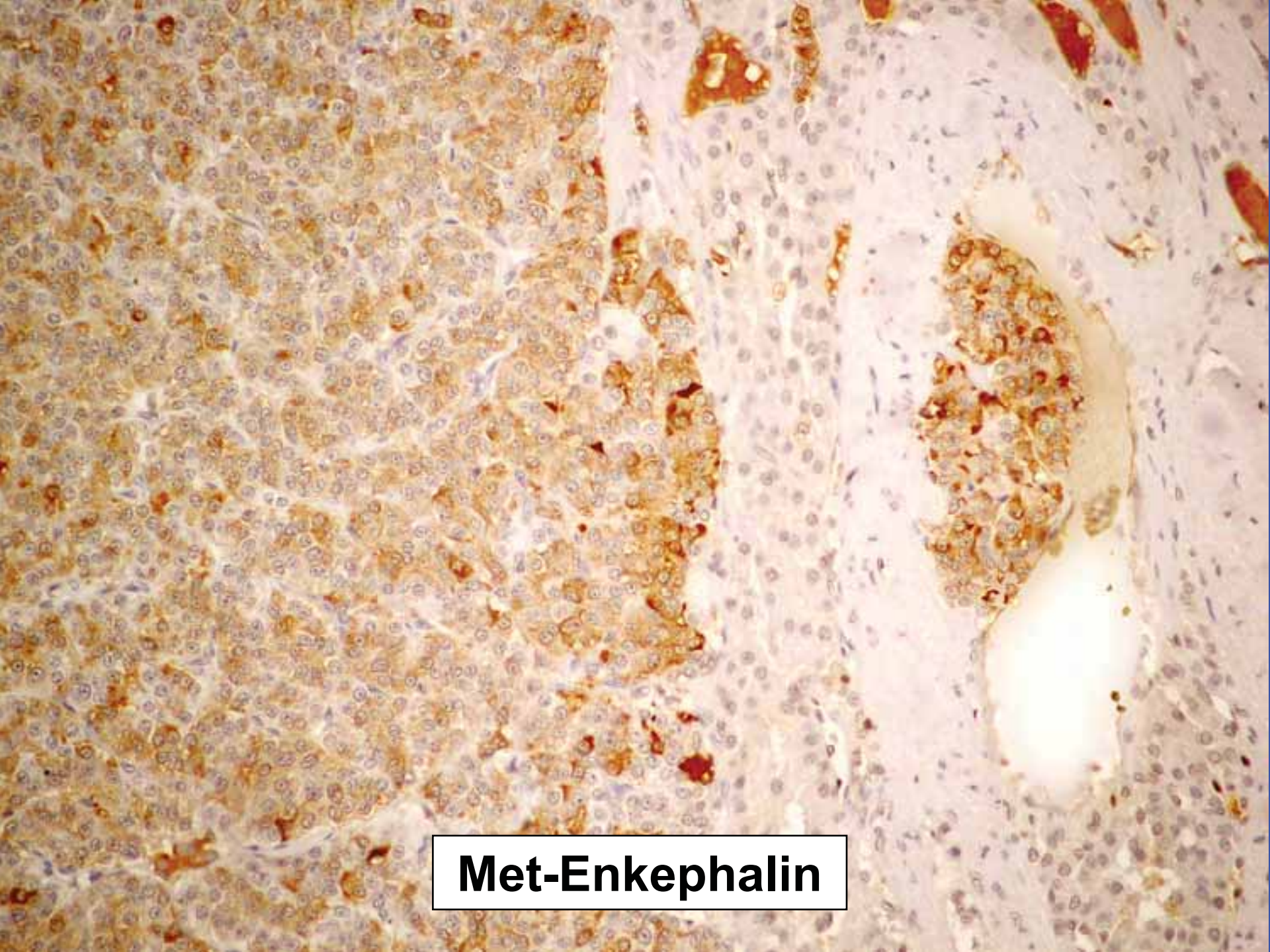




PGP9.5



Endorphin

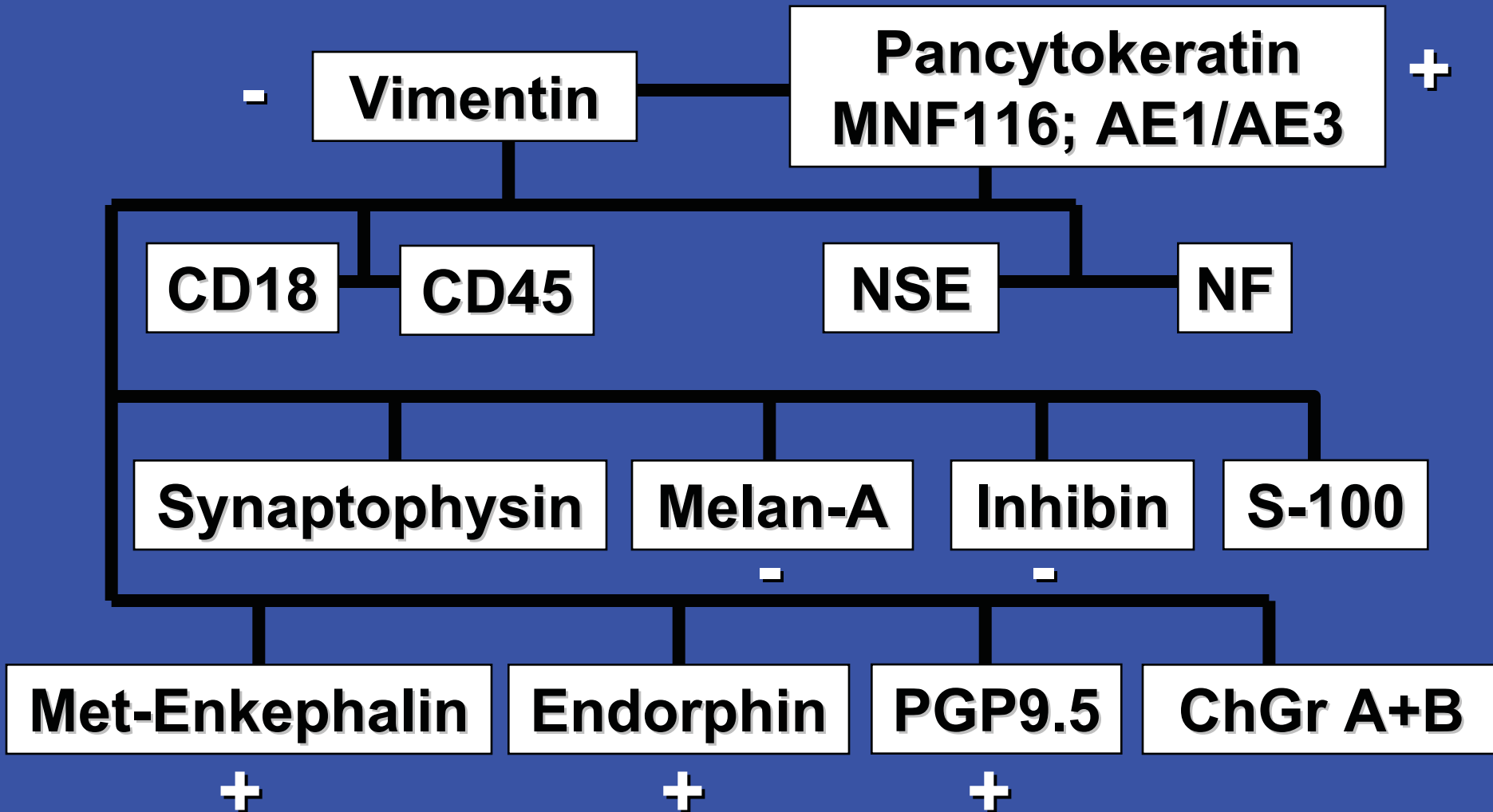


Met-Enkephalin

What's your Diagnosis



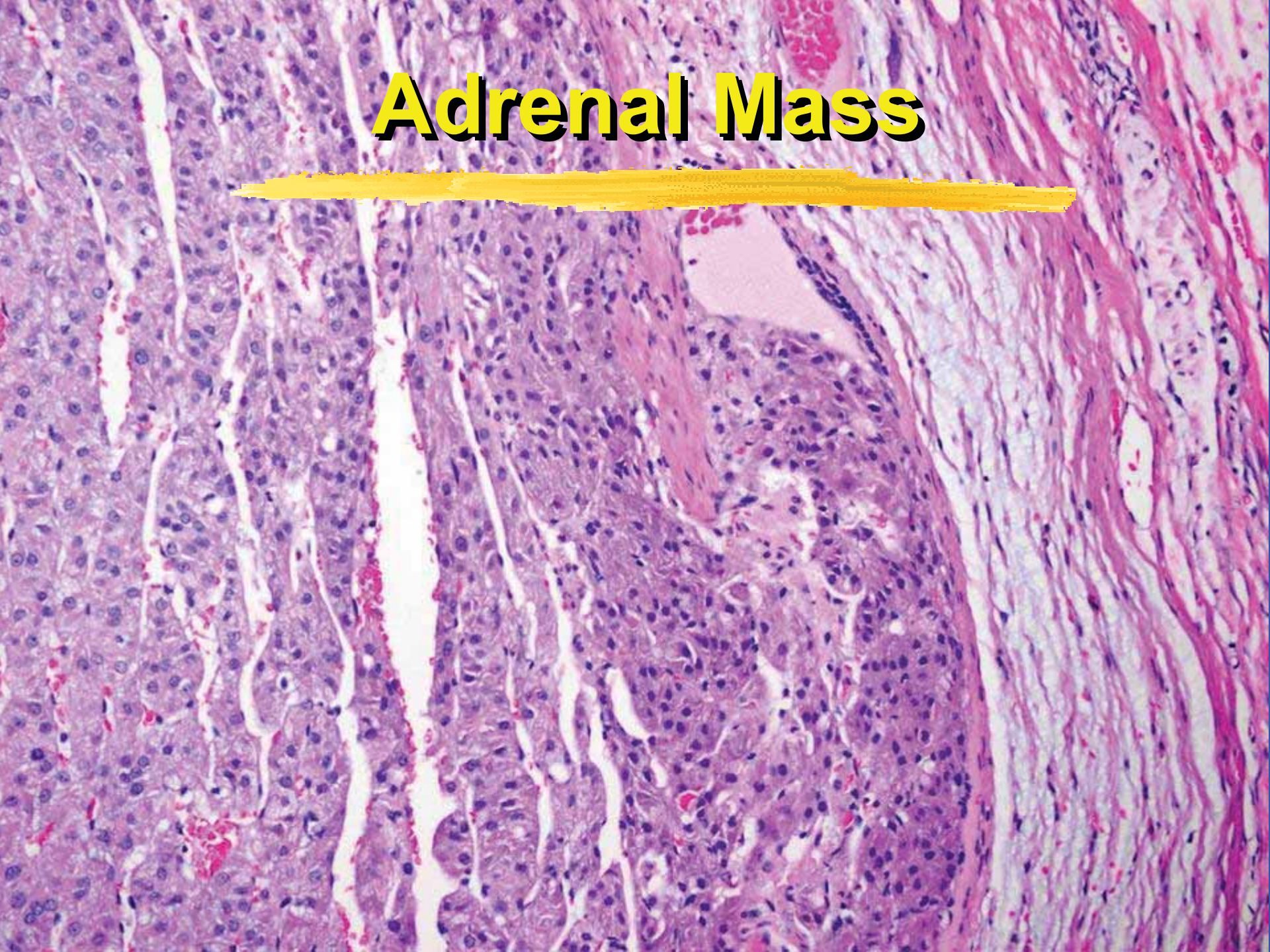
Pheochromocytoma



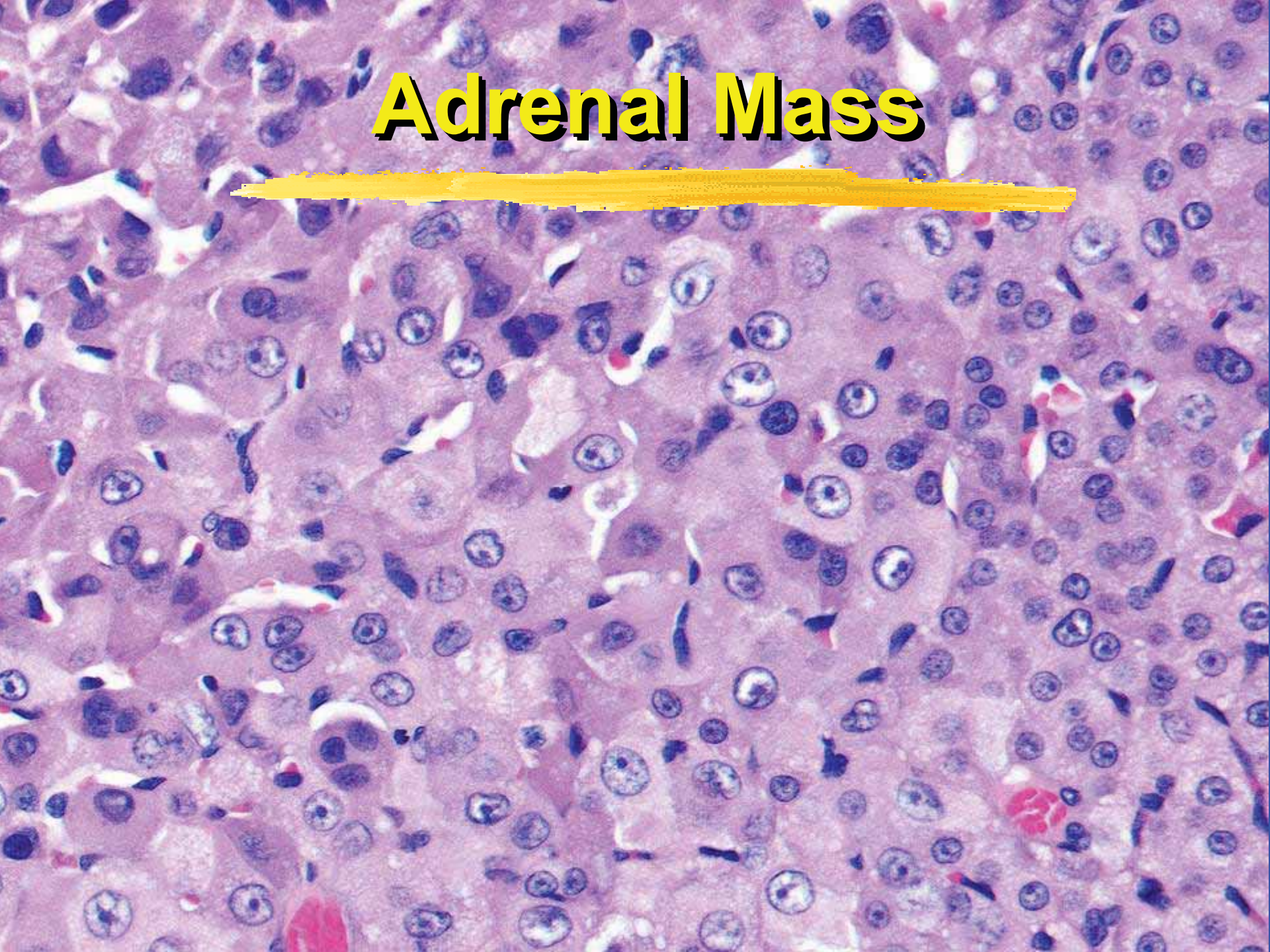
Pheochromocytomas

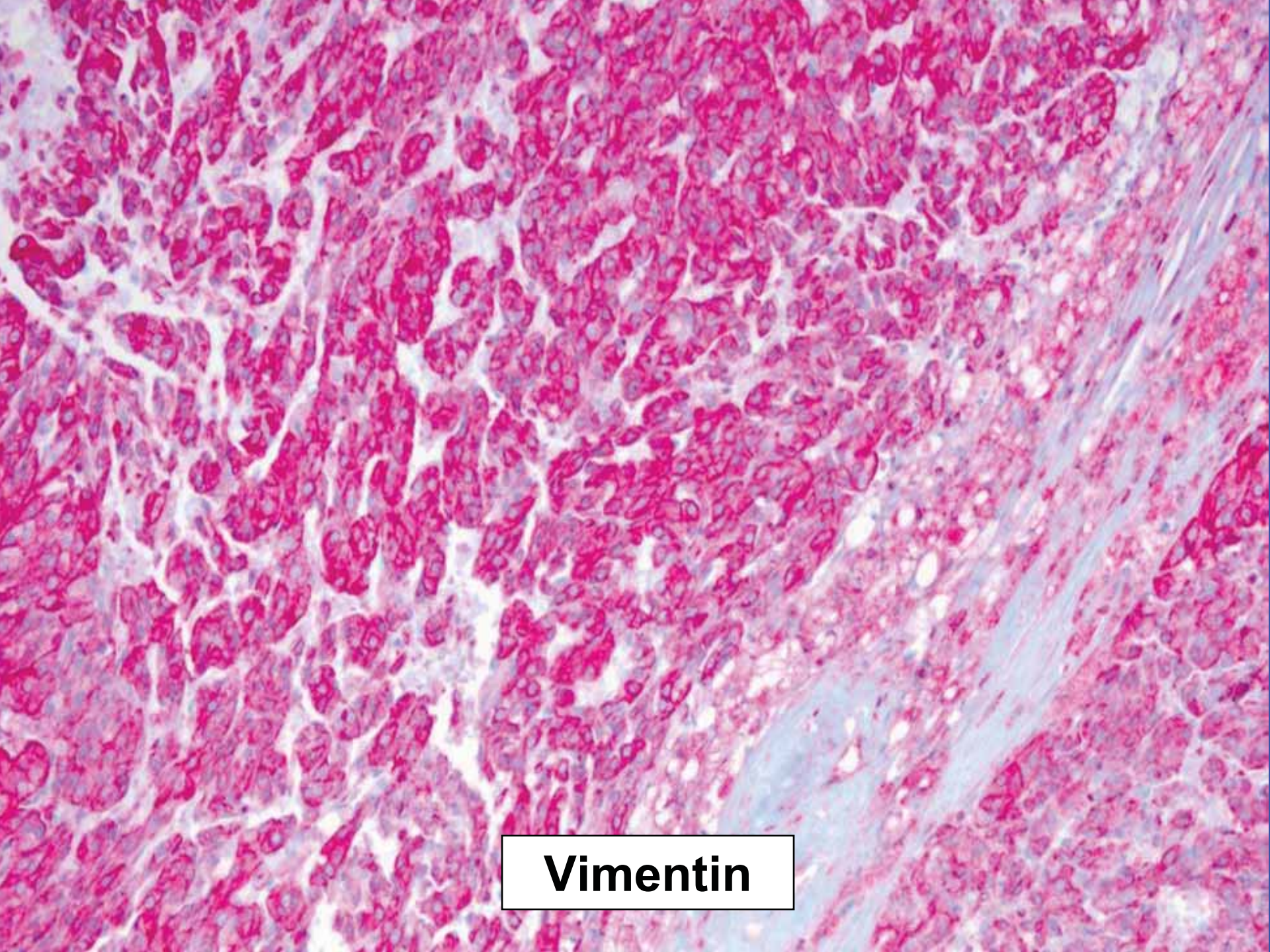
- Majority are multihormonal neoplasms
- Positive for most generic neuroendocrine marker:
 - chromogranins, synaptophysin, somatostatin, NSE, PGP 9.5, calcitonin, S-100 etc.
 - serotonin is commonly expressed
 - pancytokeratin (not paragangliomas)
 - neuropeptide Y, substance P, endorphin
- Phenylethanolamine-N-methyltransferase (PNMT):
 - converts noradrenalin to adrenalin
 - present in adrenomedullary cells
- Enkephalins: widely distributed opioid peptides
 - adrenal medulla
 - brain and peripheral nervous system
 - pheochromocytomas (PCC) and neuroblastomas
 - met-enkephalin commonly used for PCC

Adrenal Mass

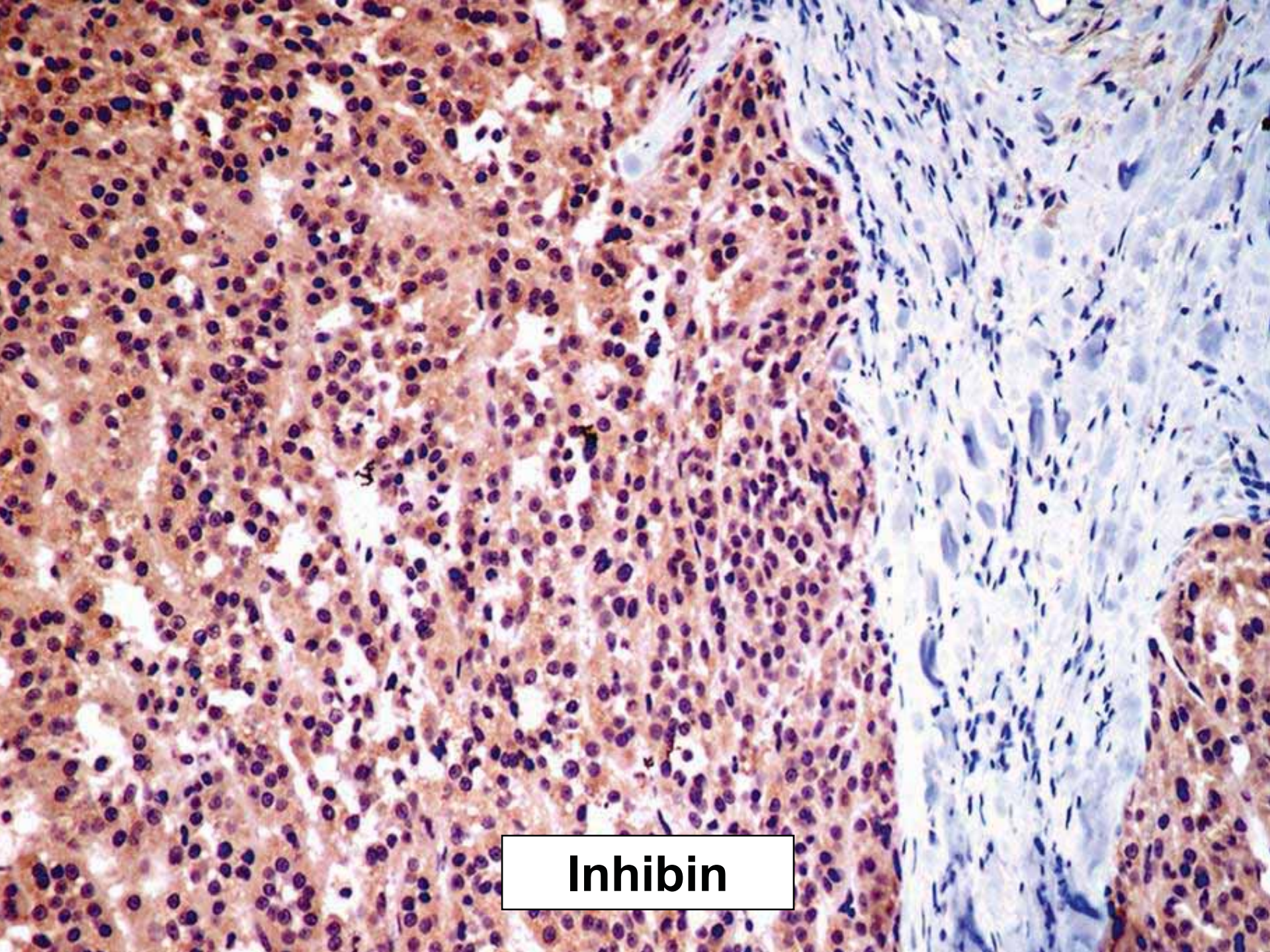


Adrenal Mass

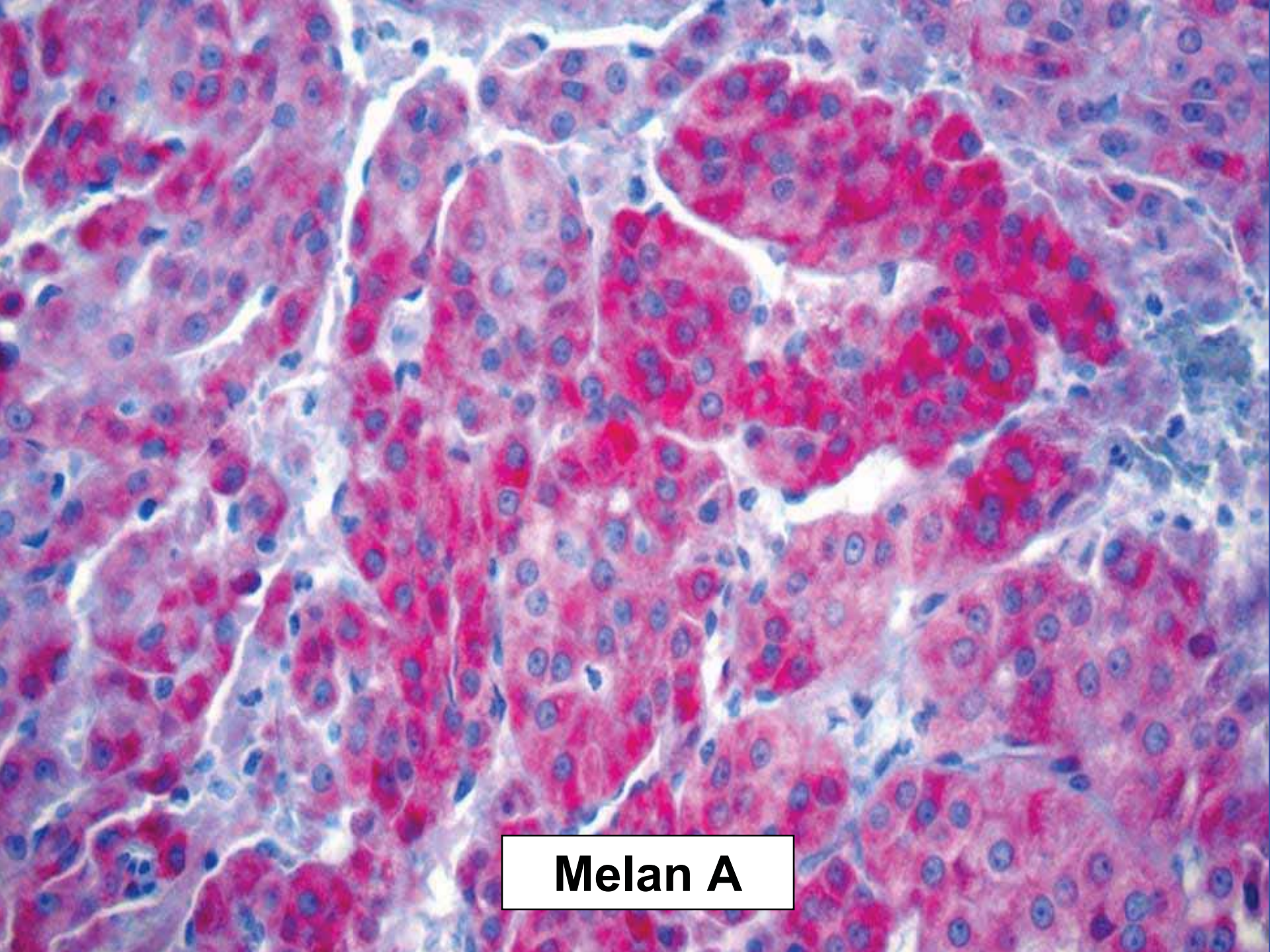




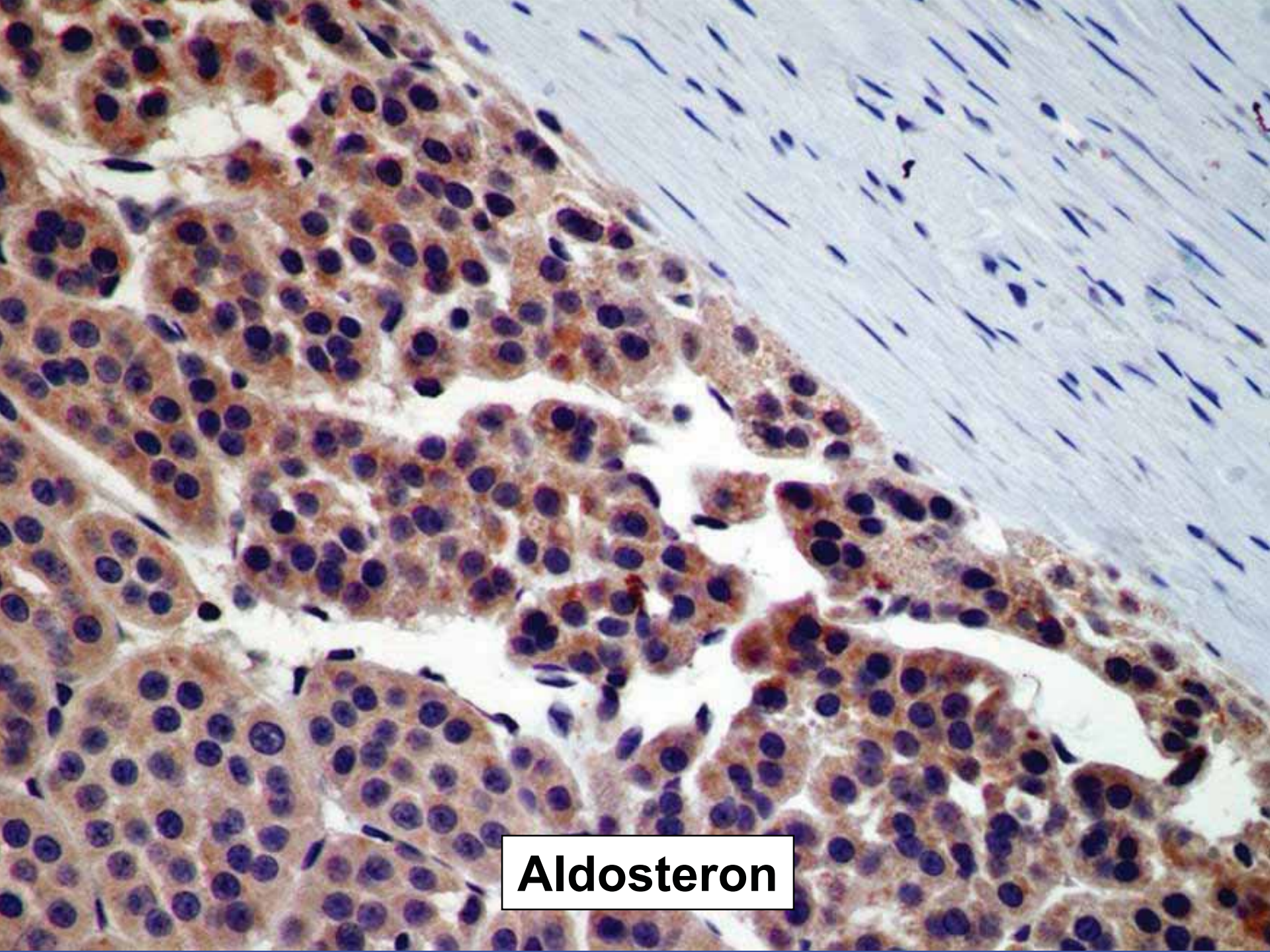
Vimentin



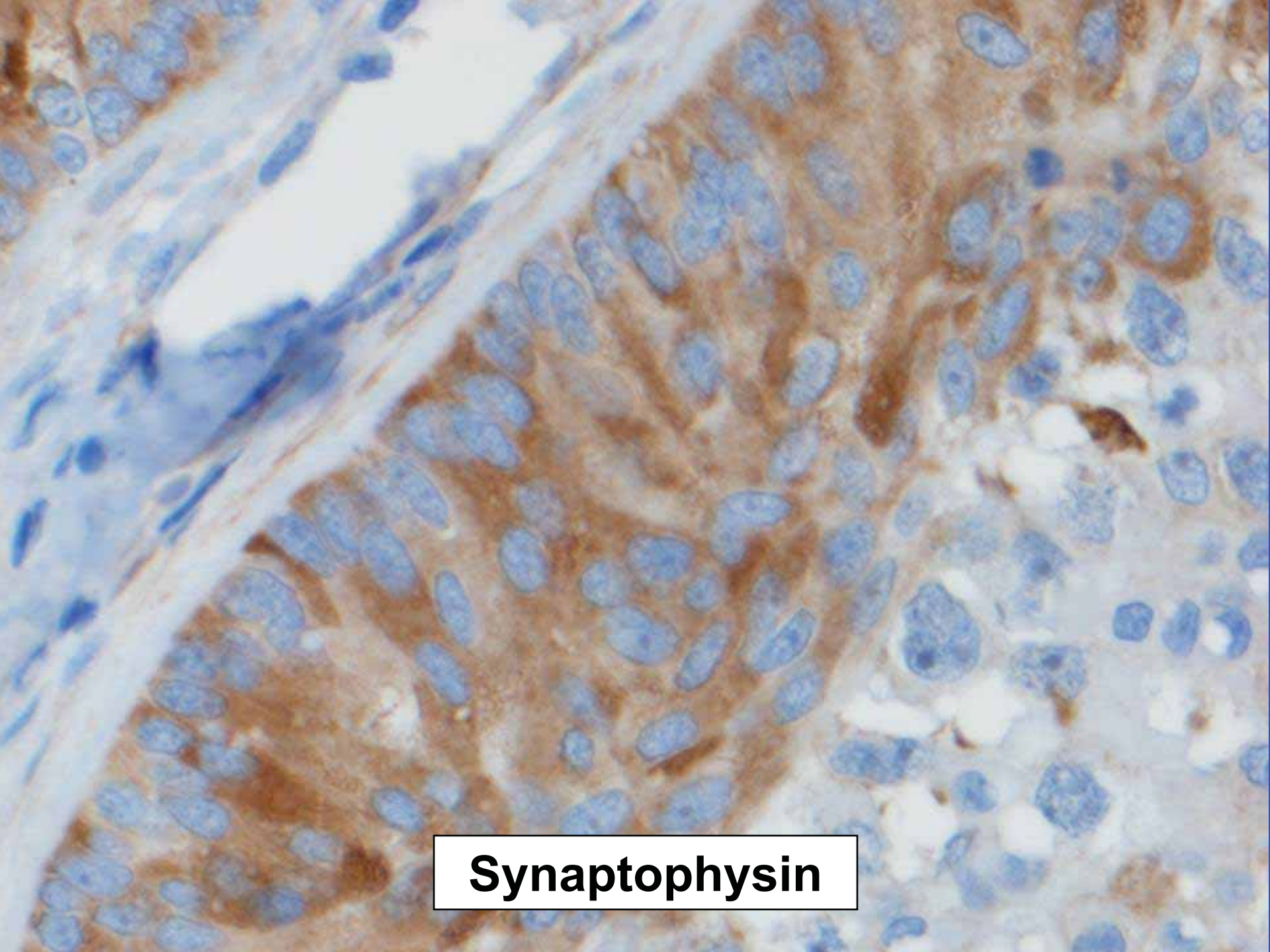
Inhibin



Melan A



Aldosteron

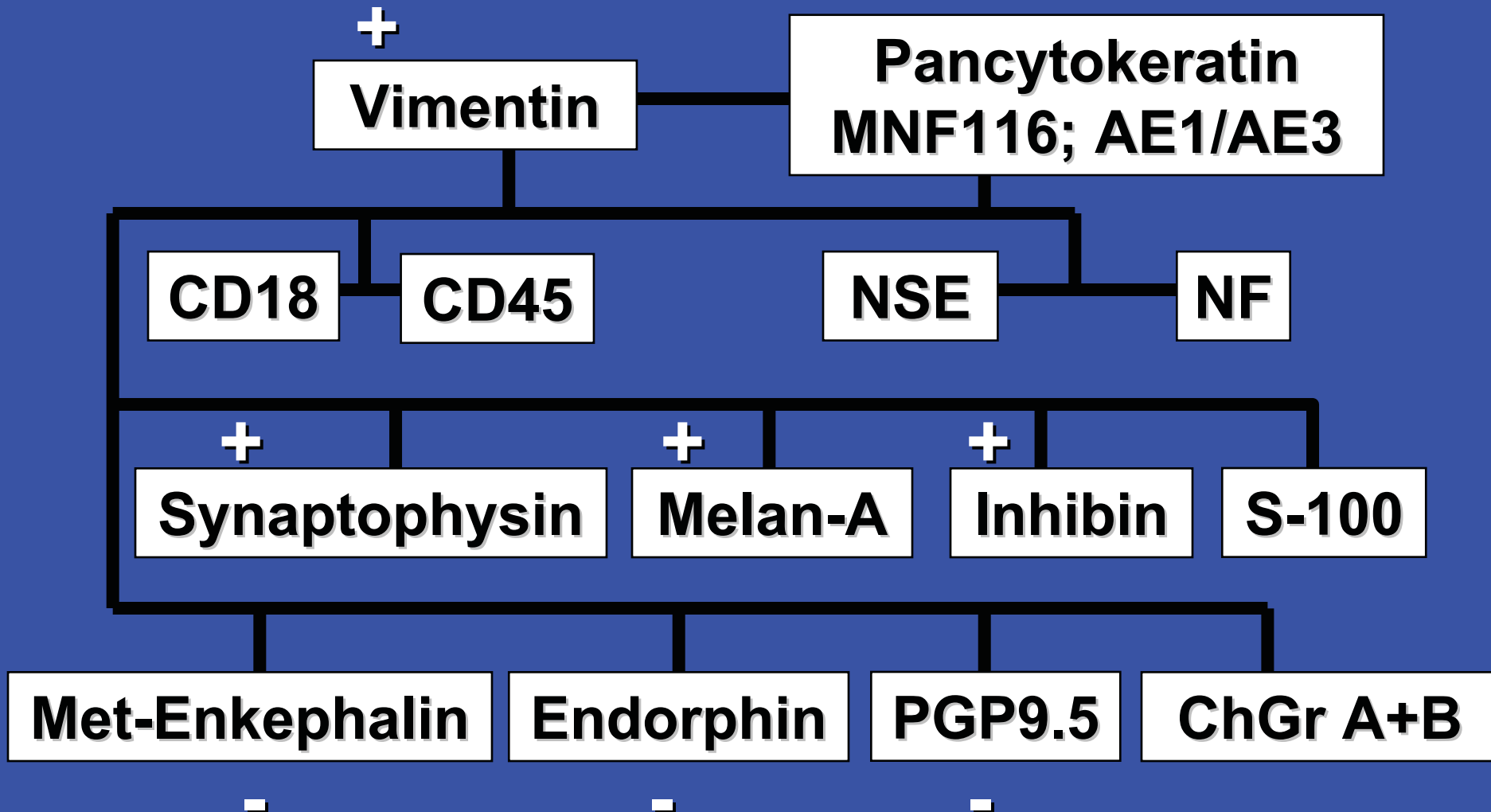


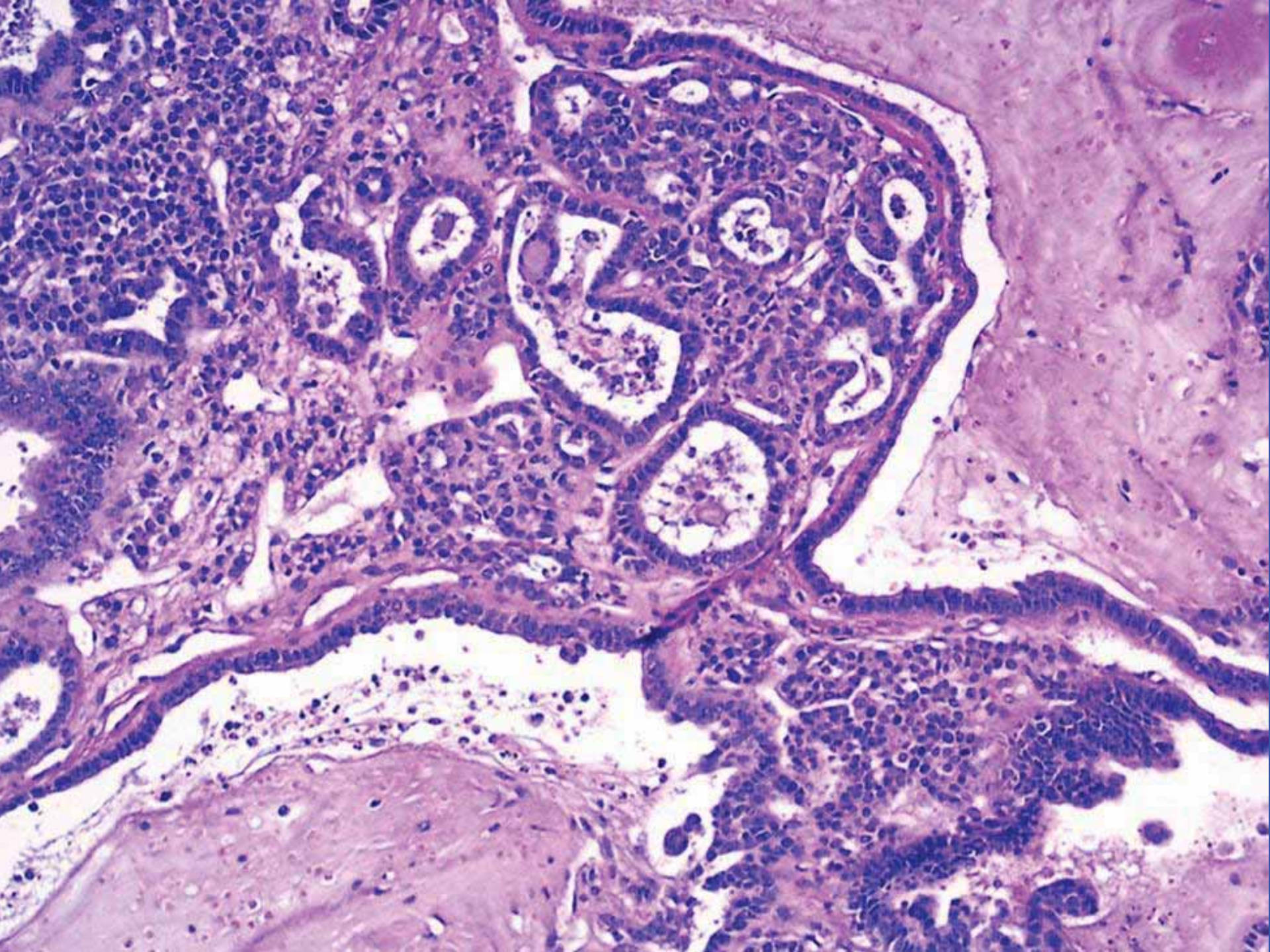
Synaptophysin

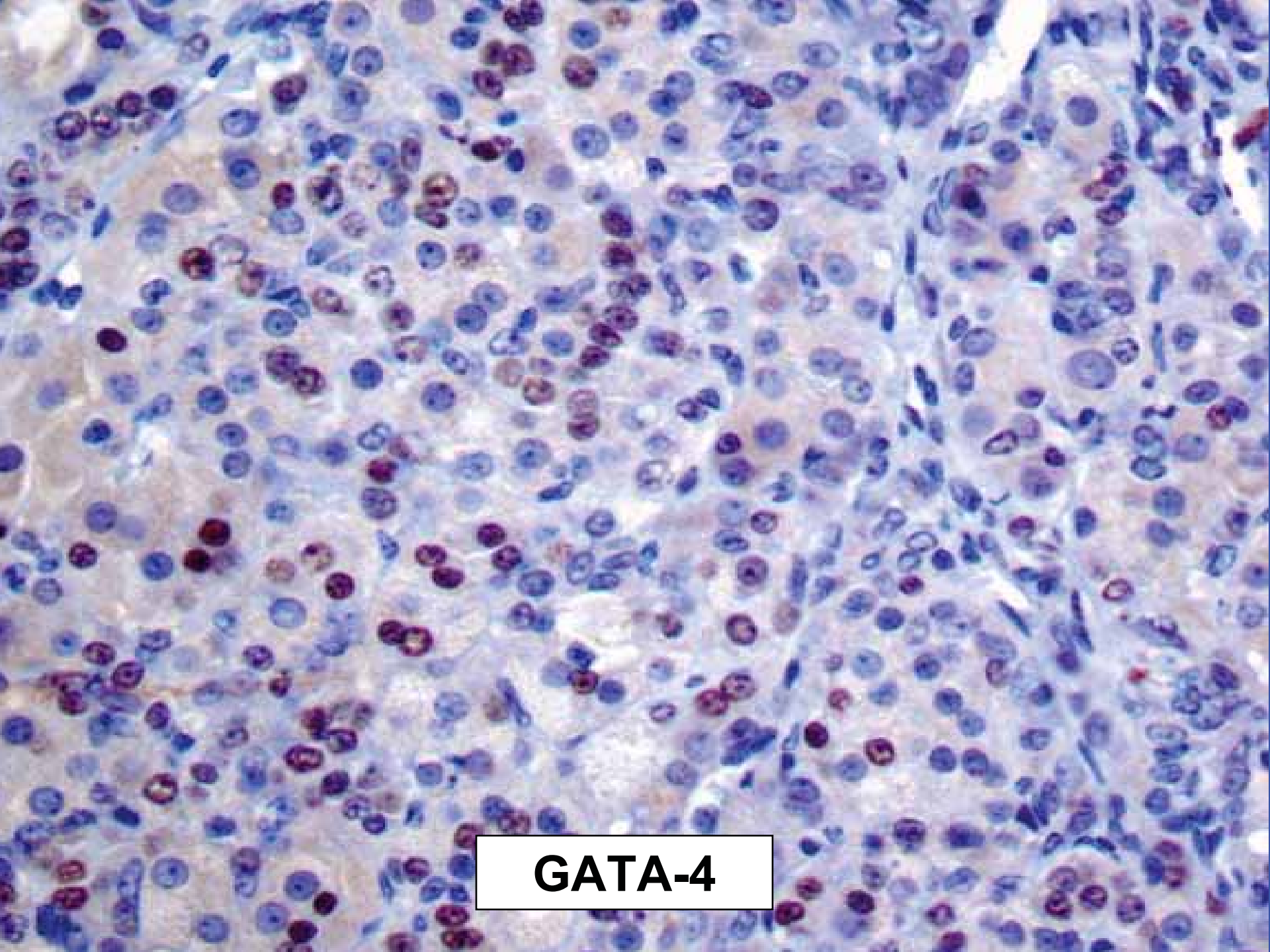
**What's
your
Diagnosis**



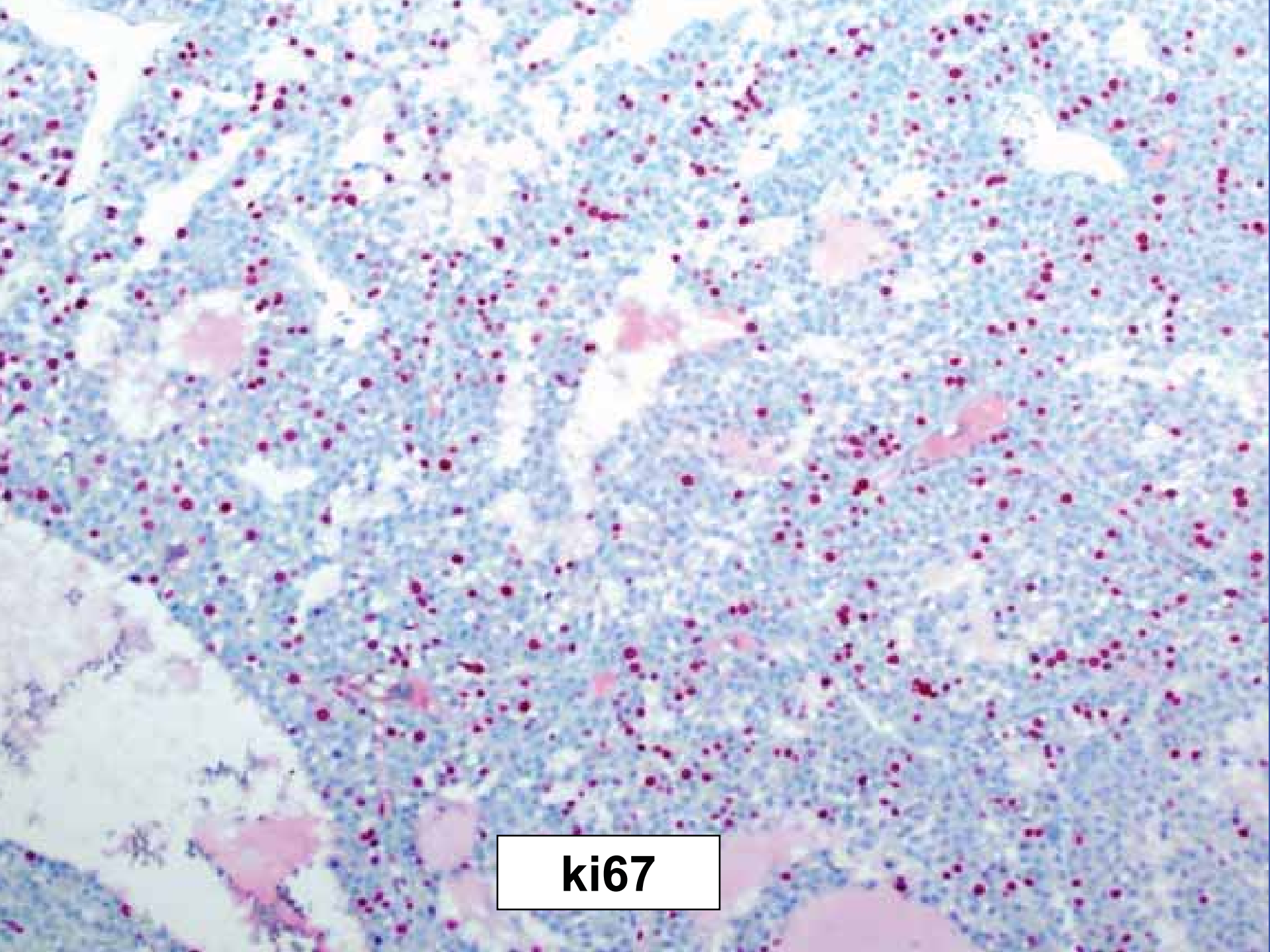
Adrenal Cortical Carcinoma







GATA-4

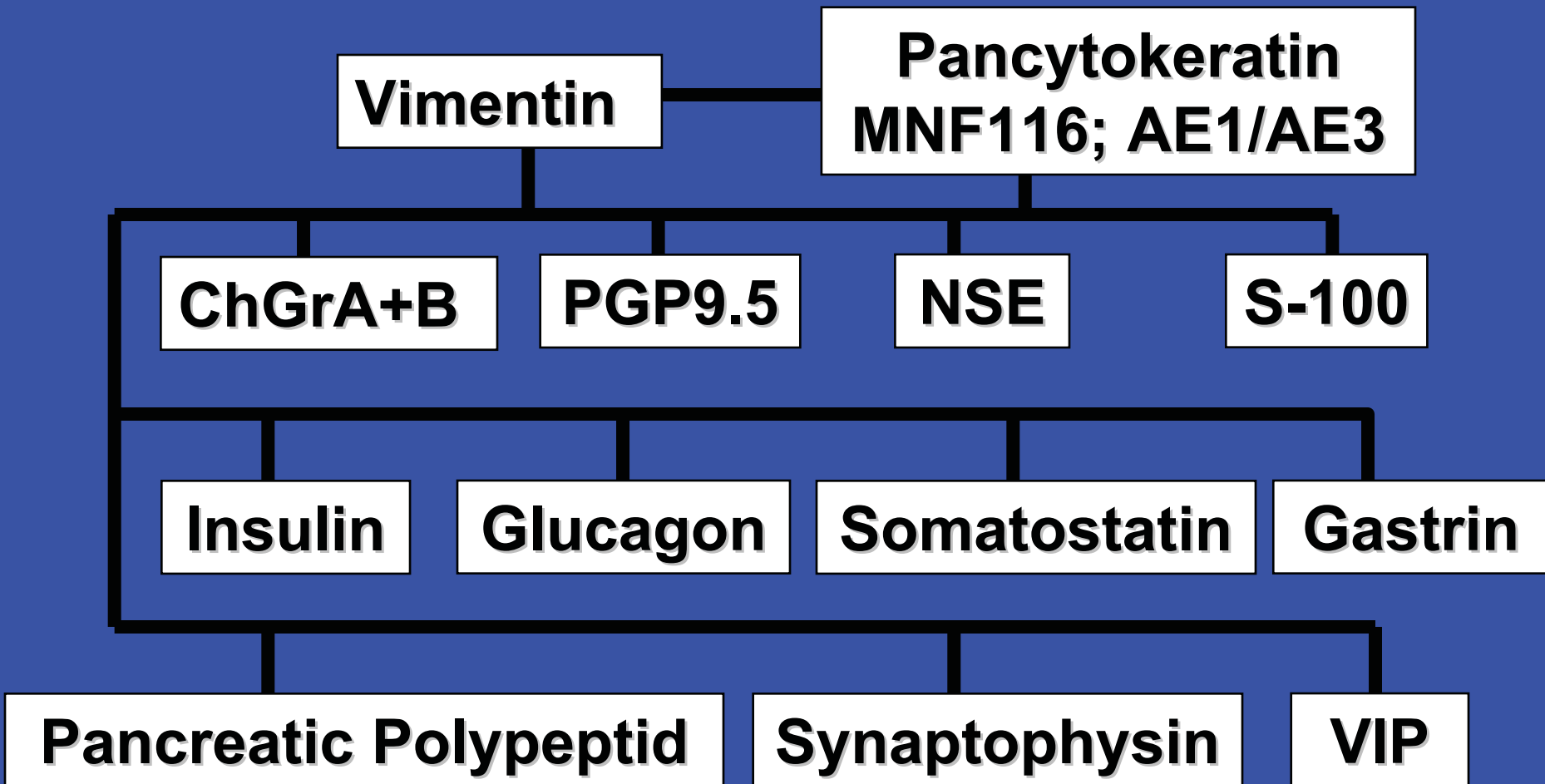


ki67

Adrenal Cortical Carcinoma

- **Vimentin:** intermediate filament positive in adrenal cortex
- **Inhibin:** gonadal sex-cord stromal cells (adrenal cortex versus medulla)
- **Melan A:** melanocytes, adrenal cortex (versus medulla), testis, ovary
- **Aldosteron:** testing of hypokalemic animals
- **Endorphin:** MSH and ACTH cells in pituitary, adrenal medulla (versus cortex)
- **Ki67 and GATA-4:** Higher degree of anaplasia associated with increased expression

Tumors of the Pancreas



Endocrine Pancreas

- Pancreatic islet cell tumors contain various biological important factors, are frequently functional and multihormonal
- In humans often component of MEN1
- Functioning Tumors:
 - eutopic hormone production
 - insulin (insulinoma)
 - glucagon (glucagonoma)
 - somatostatin (somatostatinoma)
 - pancreatic polypeptide
 - ectopic hormone production
 - gastrin (gastrinoma)
 - vasoactive intestinal peptide (VIP)
 - growth hormone releasing hormone
- Behavior is commonly related to hormones they produce

Glucagon



- A-cells of the endocrine pancreas have strong cytoplasmic staining
- A-cells also contain chromogranins, glicentin-related pancreatic peptide, and major proglucagon fragment
- Primary use: diagnosis of glucagonomas
 - may also contain pancreatic polypeptide, insulin, somatostatin
 - associated with diabetes mellitus, necrolytic dermatitis
- Also present in extrainsular cells in pancreatic ducts

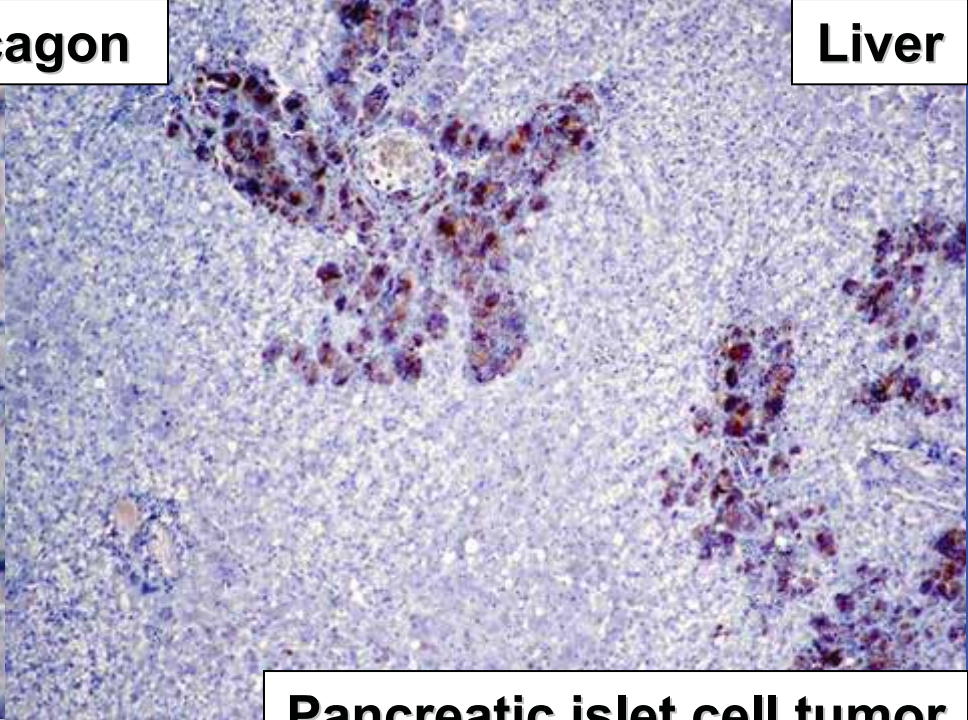
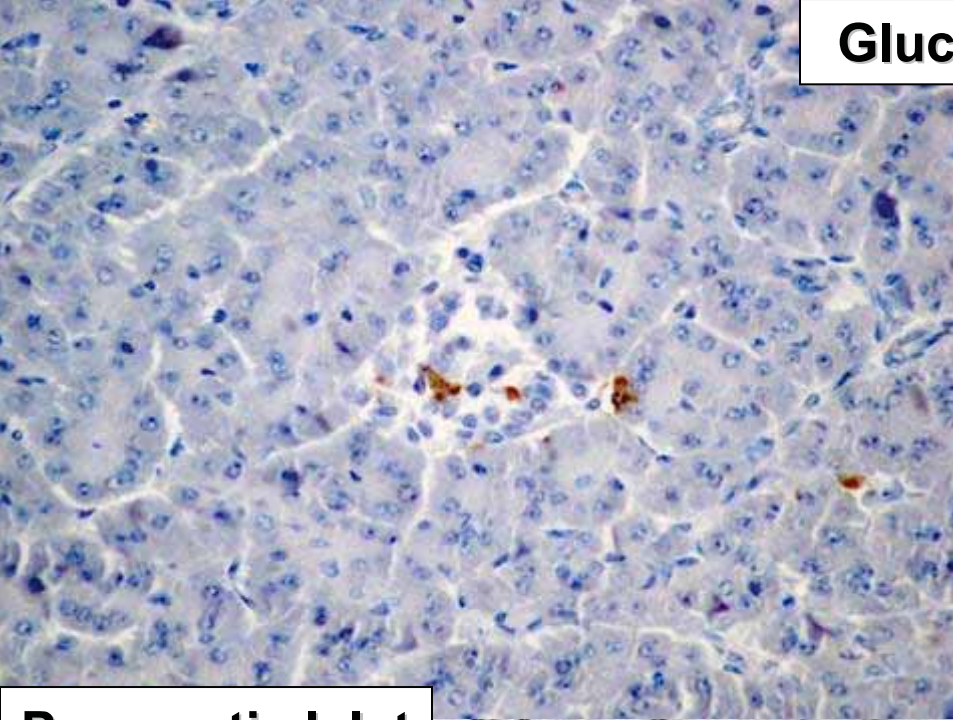
Insulin



- Beta-cells of the endocrine pancreas have strong cytoplasmic staining.
- B-cells are the most numerous endocrine pancreatic cells and also contain proinsulin, chromogranin A, and islet amyloid peptide
- Primary use: diagnosis of insulinomas
 - may also contain pancreatic polypeptide, gastrin, glucagon, somatostatin, ACTH
 - approximately 50% are multihormonal
 - associated with hypoglycemia

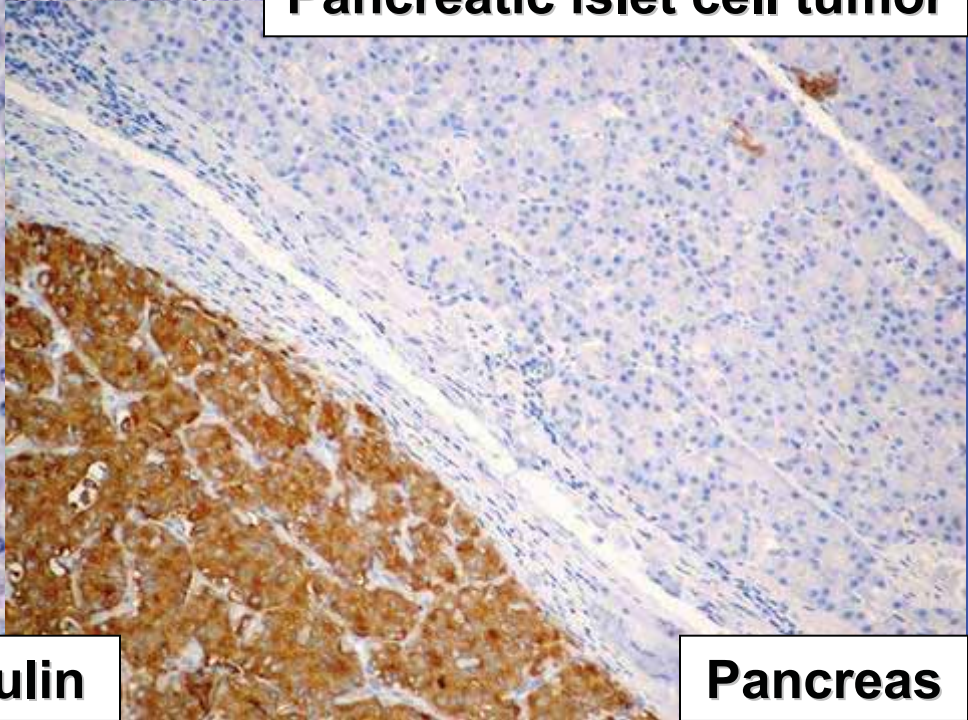
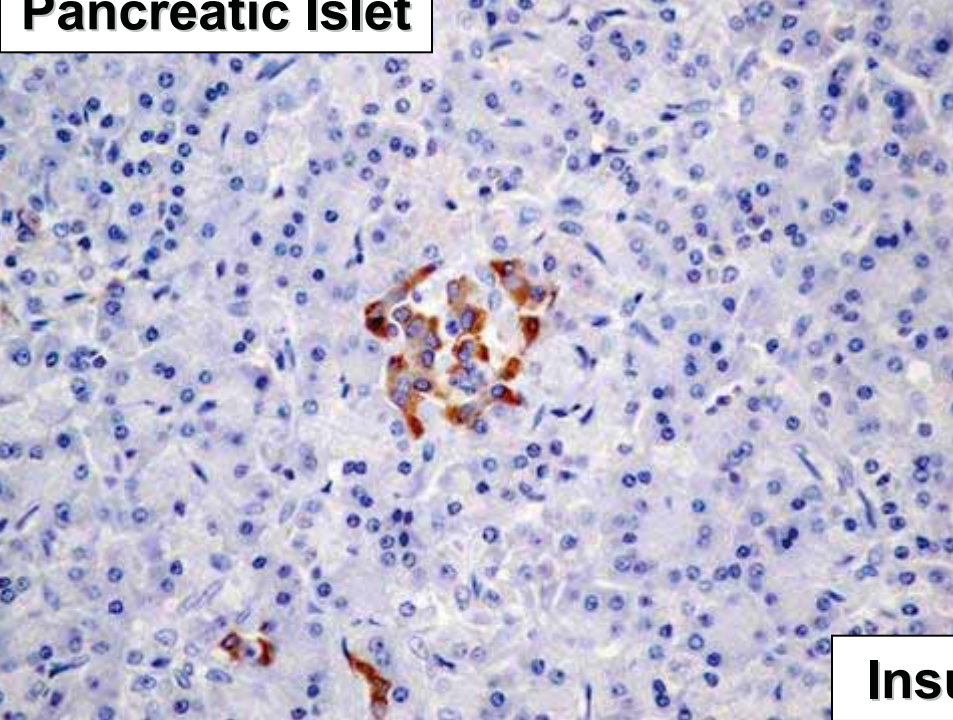
Glucagon

Liver



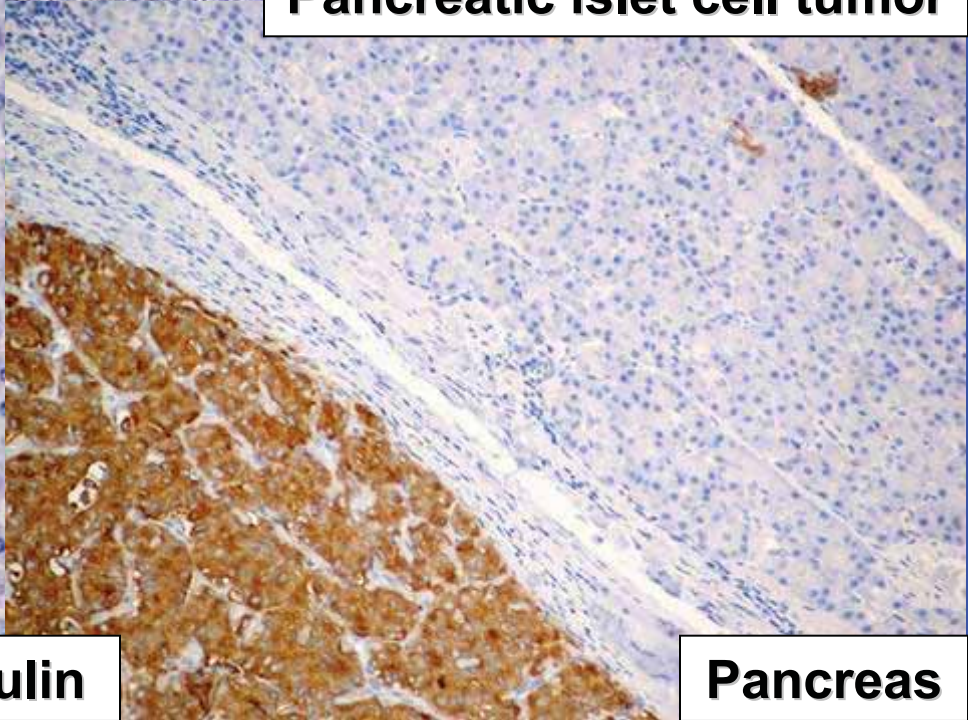
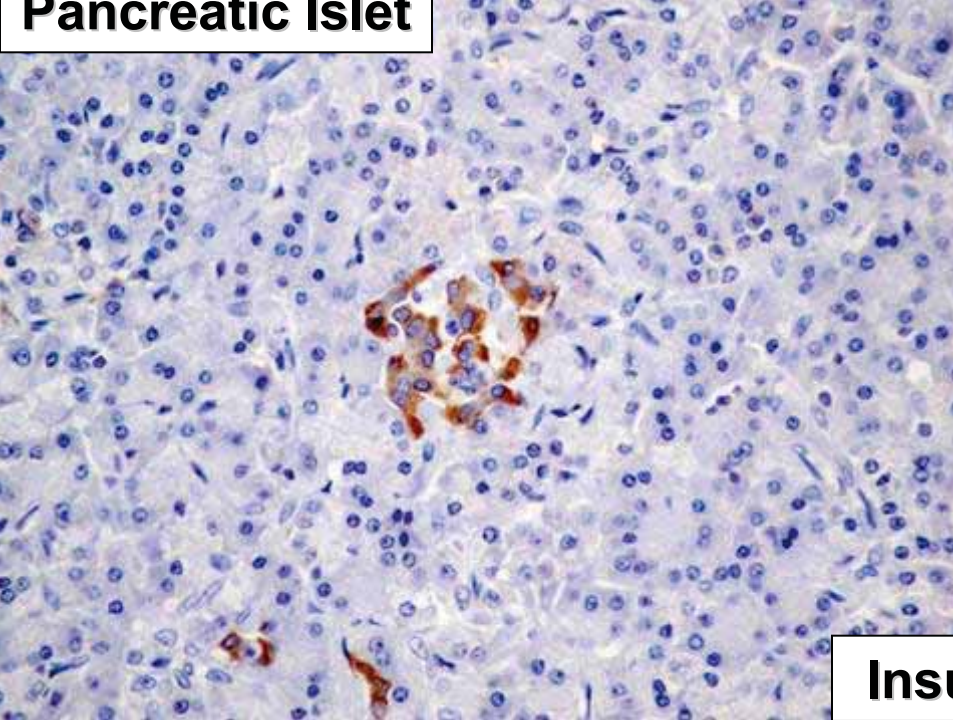
Pancreatic Islet

Pancreatic islet cell tumor



Insulin

Pancreas

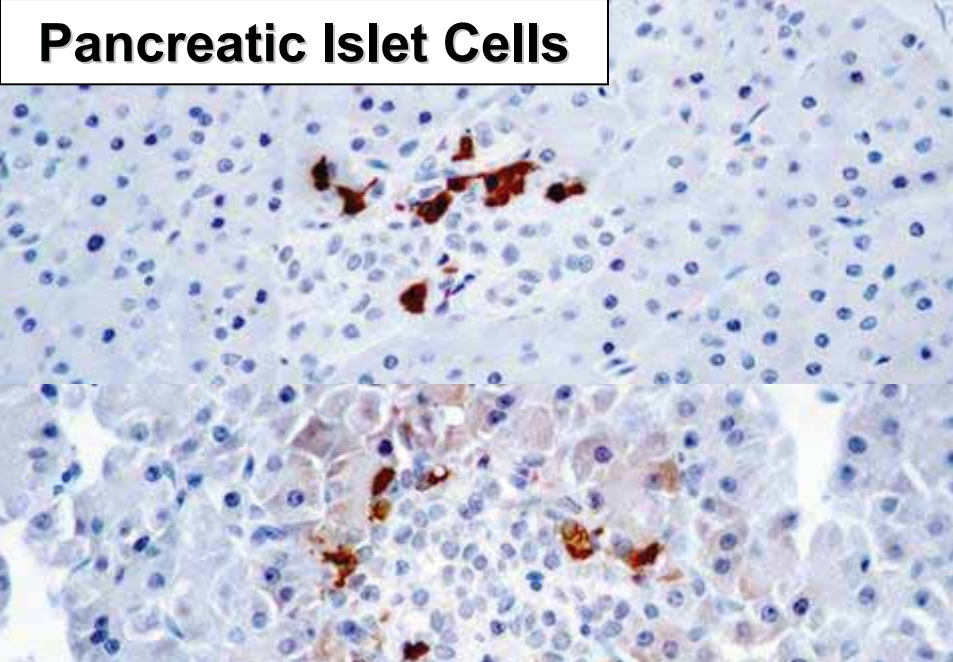


Somatostatin

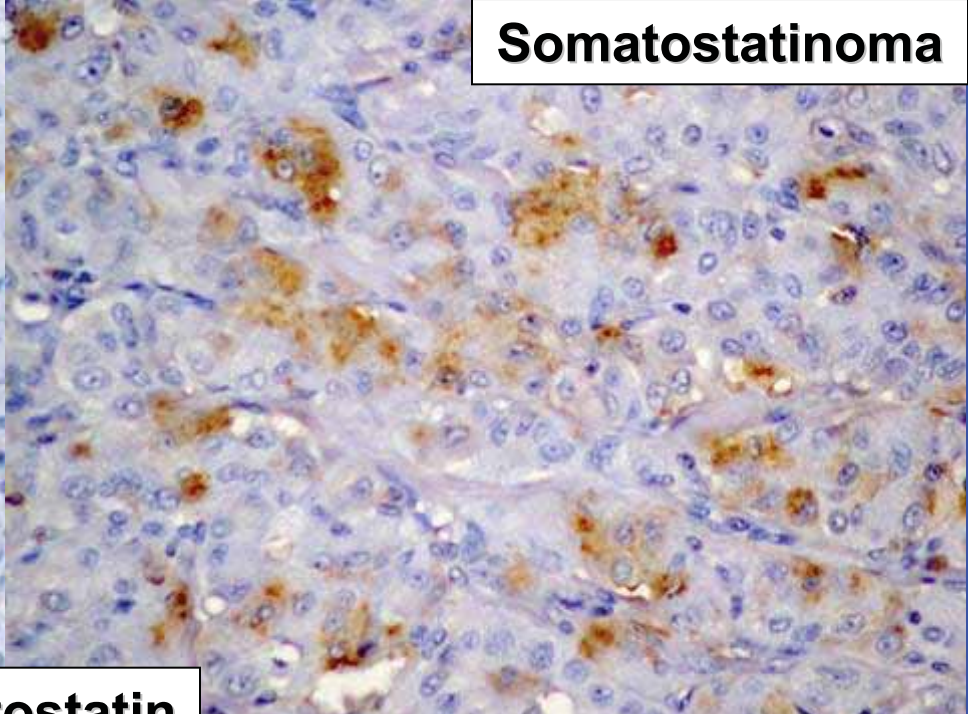


- D-cells of the endocrine pancreas have strong cytoplasmic staining
- Functions as an inhibitory hormone of the neuroendocrine system
- Primary use: diagnosis of somatostatinomas
 - may also contain pancreatic polypeptide, gastrin, ACTH and calcitonin
 - associated with diabetes mellitus, steatorrhea, hypochlorhydria in humans
- Also present in c-cell carcinomas/hyperplasia, pheochromocytomas, pulmonary carcinoids, thymic tumors

Pancreatic Islet Cells

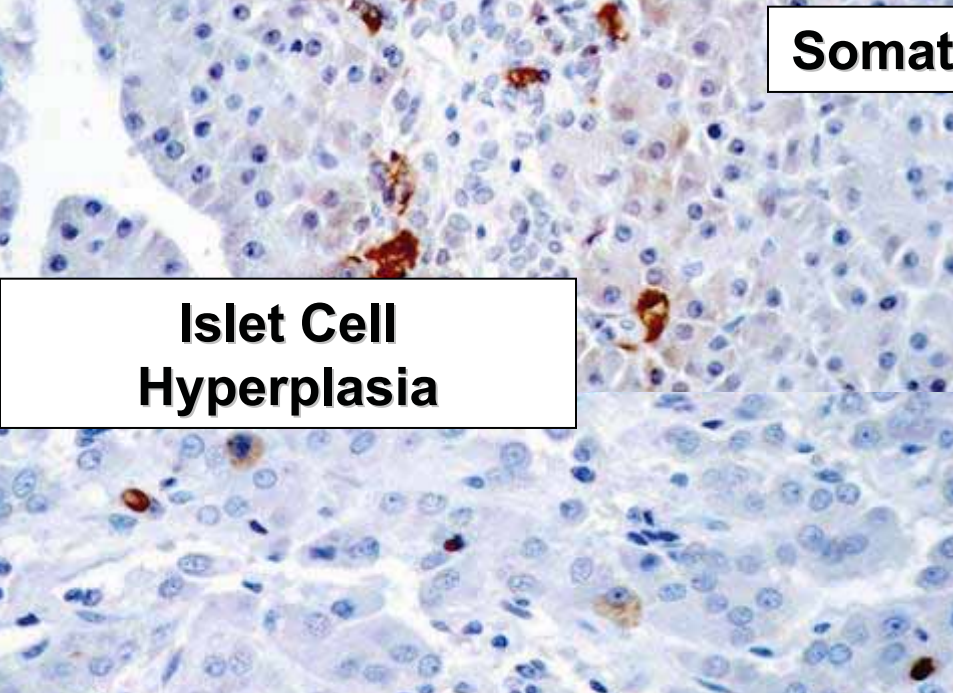


Somatostatinoma



Somatostatin

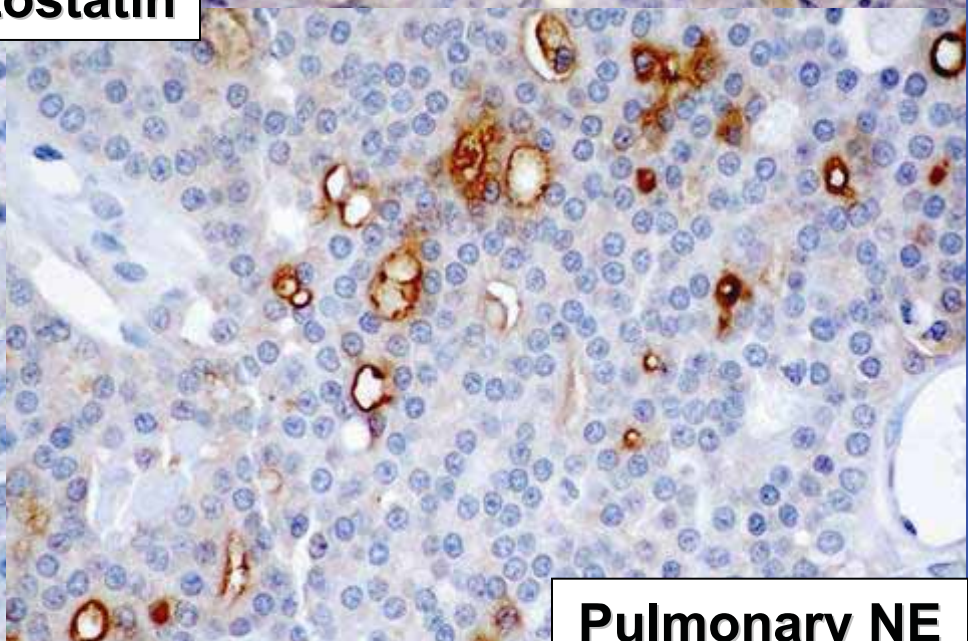
**Islet Cell
Hyperplasia**



Pheochromocytoma



**Pulmonary NE
Carcinoma**

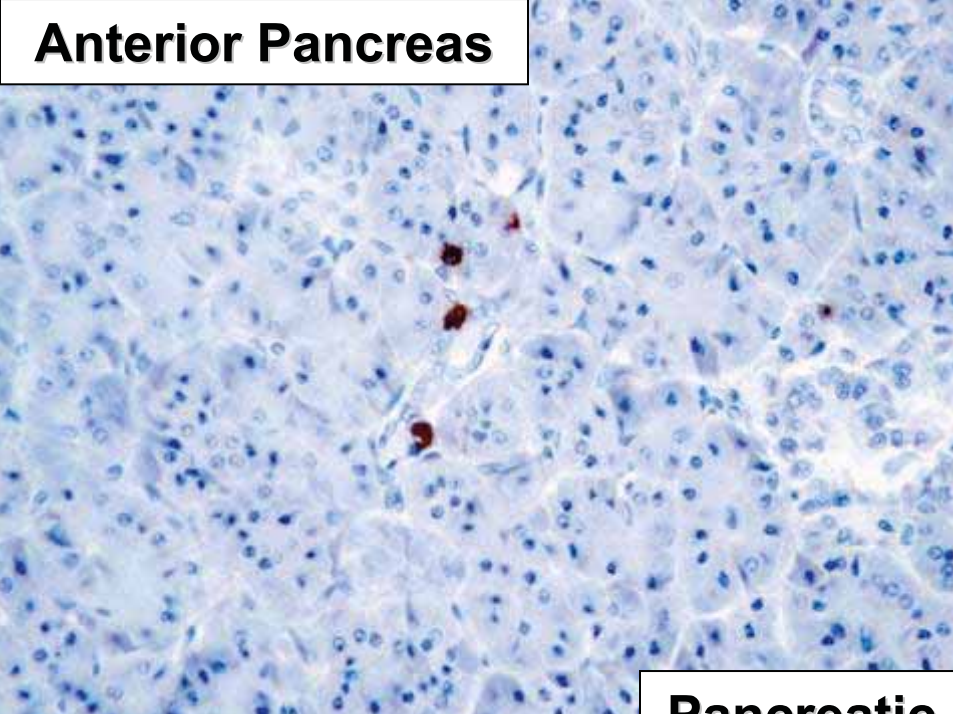


Pancreatic Polypeptide

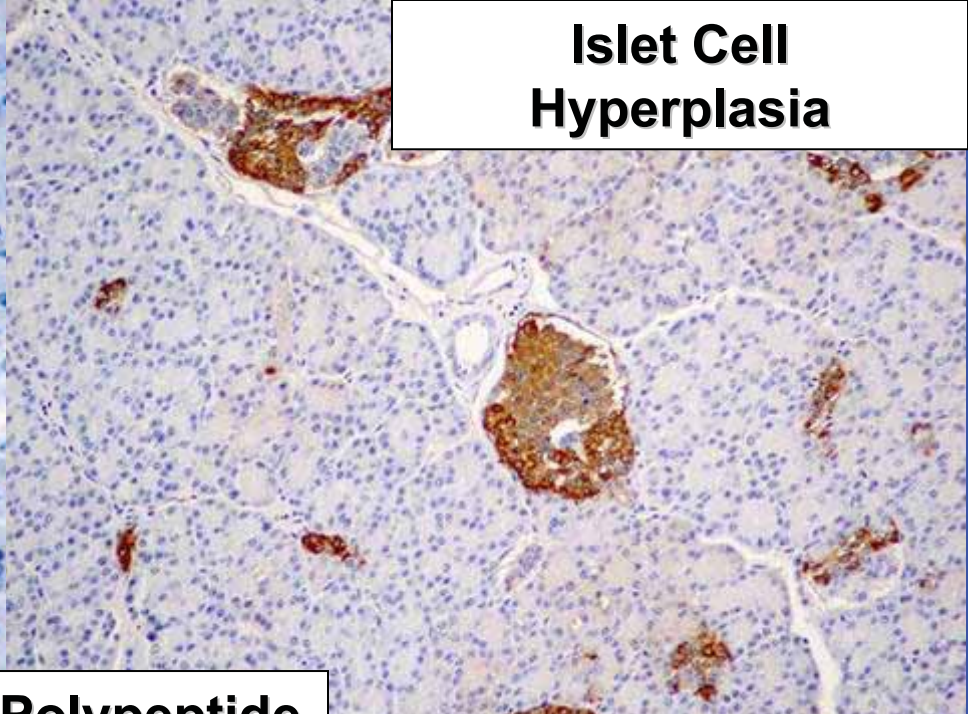


- F-cells of the endocrine pancreas, cells in small pancreatic ducts, and focal acinar cells have strong cytoplasmic staining.
- Present in 70% of endocrine cells of the posterior pancreas and 5% of the remaining islets
- Approximately 10% of pancreatic endocrine cells are present in extrainsular sites, distributed among ductual and paraductular acinar cells
- Primary use: diagnosis of islet cell tumors
 - may also contain other pancreatic hormones: insulin, gastrin, ACTH and calcitonin
 - associated with diabetes mellitus, steatorrhea, hypochlorhydria in humans

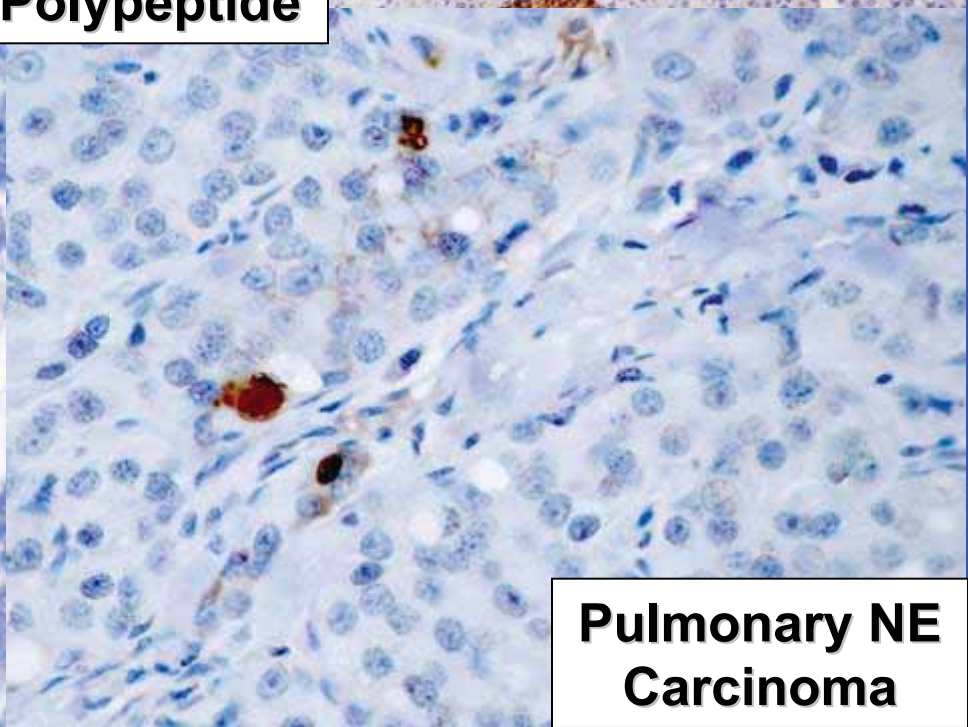
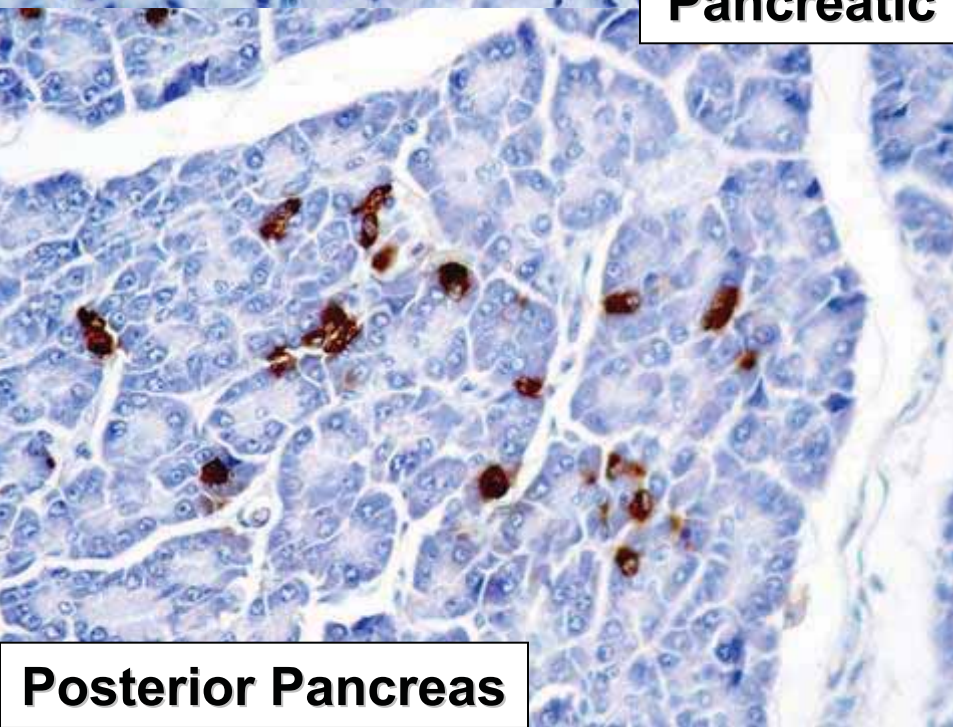
Anterior Pancreas



**Islet Cell
Hyperplasia**



Pancreatic Polypeptide



**Pulmonary NE
Carcinoma**

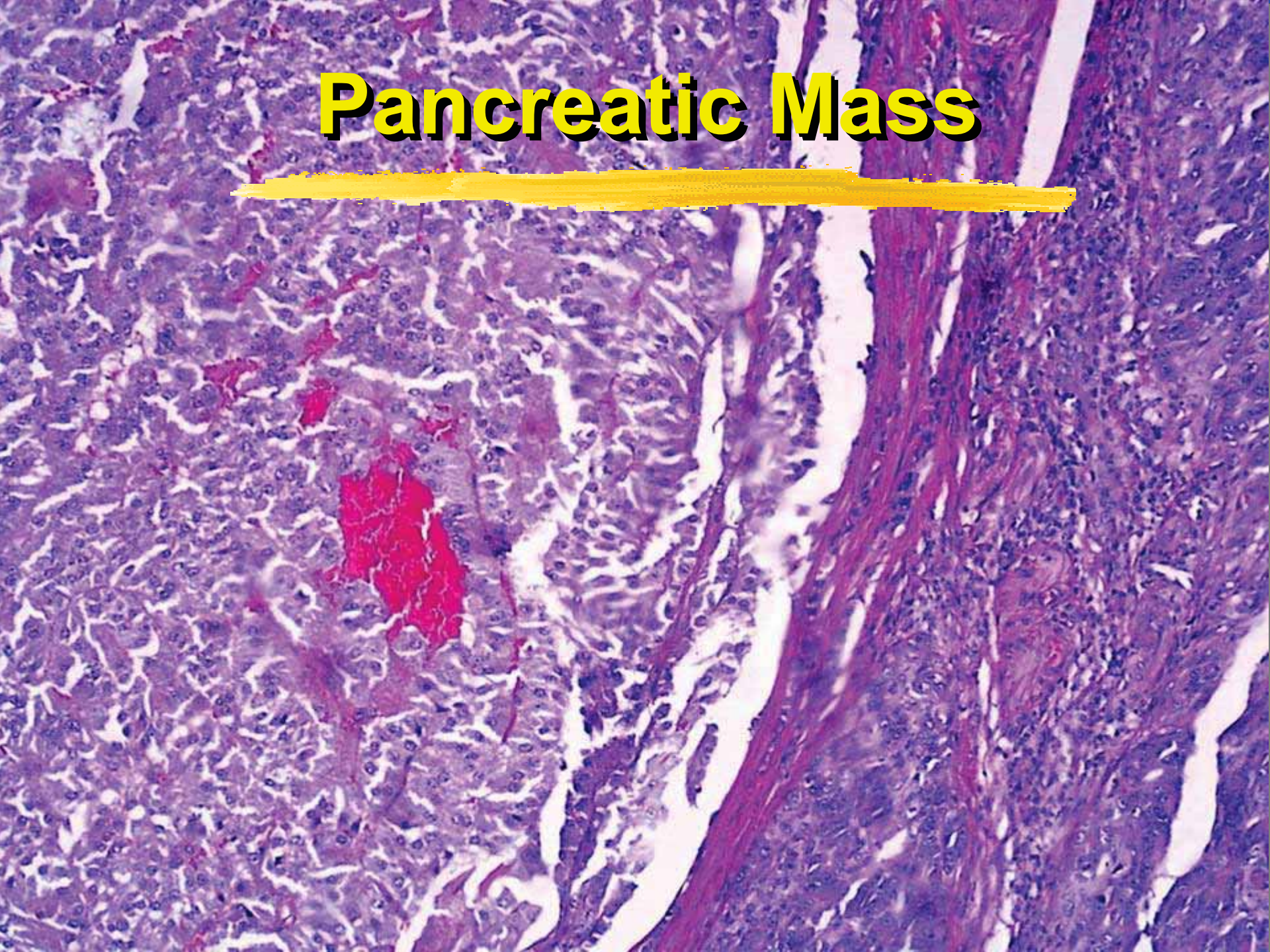
Posterior Pancreas

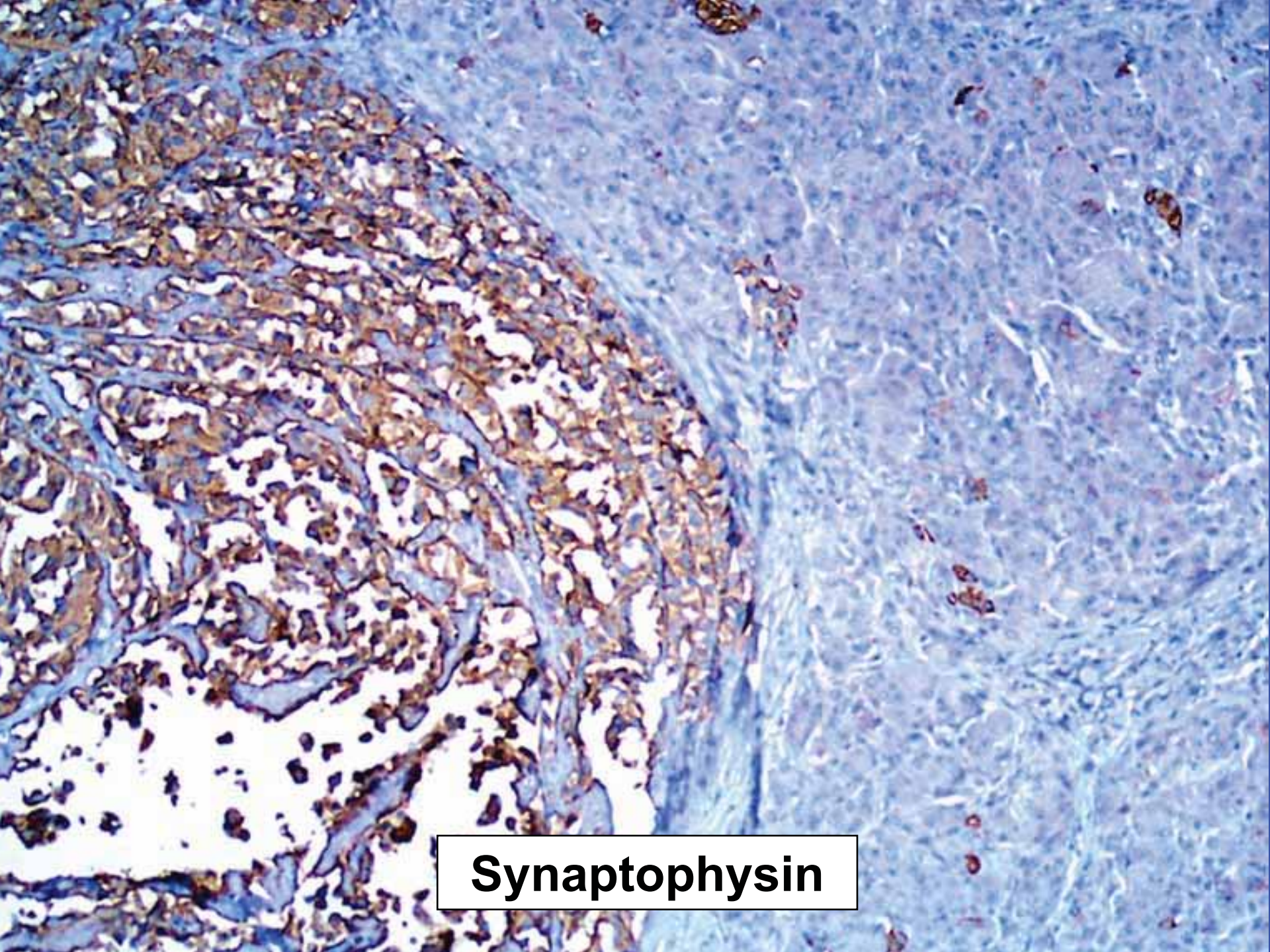
Gastrin



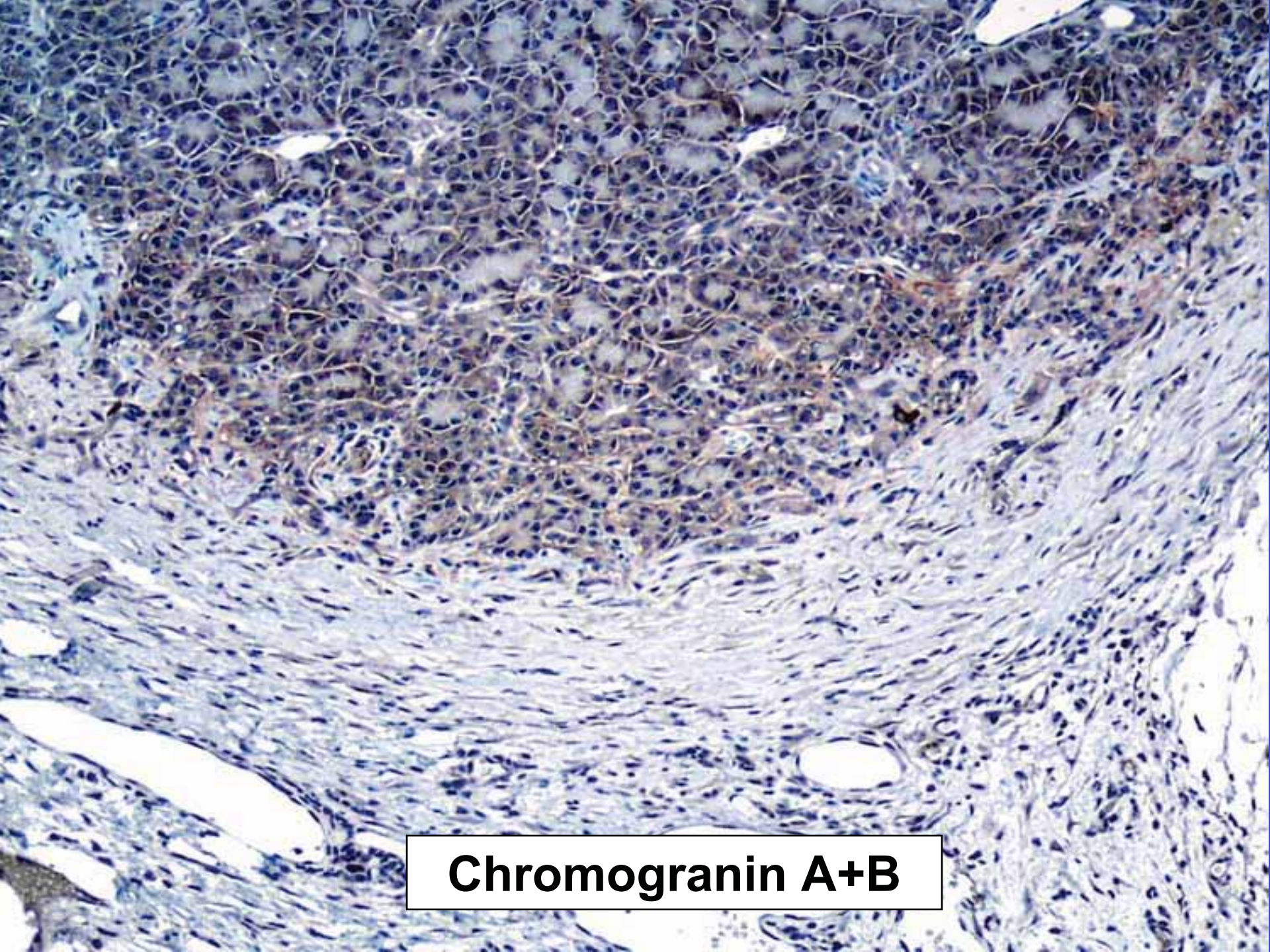
- reacts with sulfated and non-sulfated forms of gastrin-17 as well as gastrin-34
- detects gastrin producing cells in duodenum and gastric antrum
- Primary use: diagnosis of gastrinomas
 - may also contain pancreatic polypeptide, frequently multihormonal
 - gastrinomas can metastasize to the liver
 - associated with Zollinger-Ellison Syndrome

Pancreatic Mass

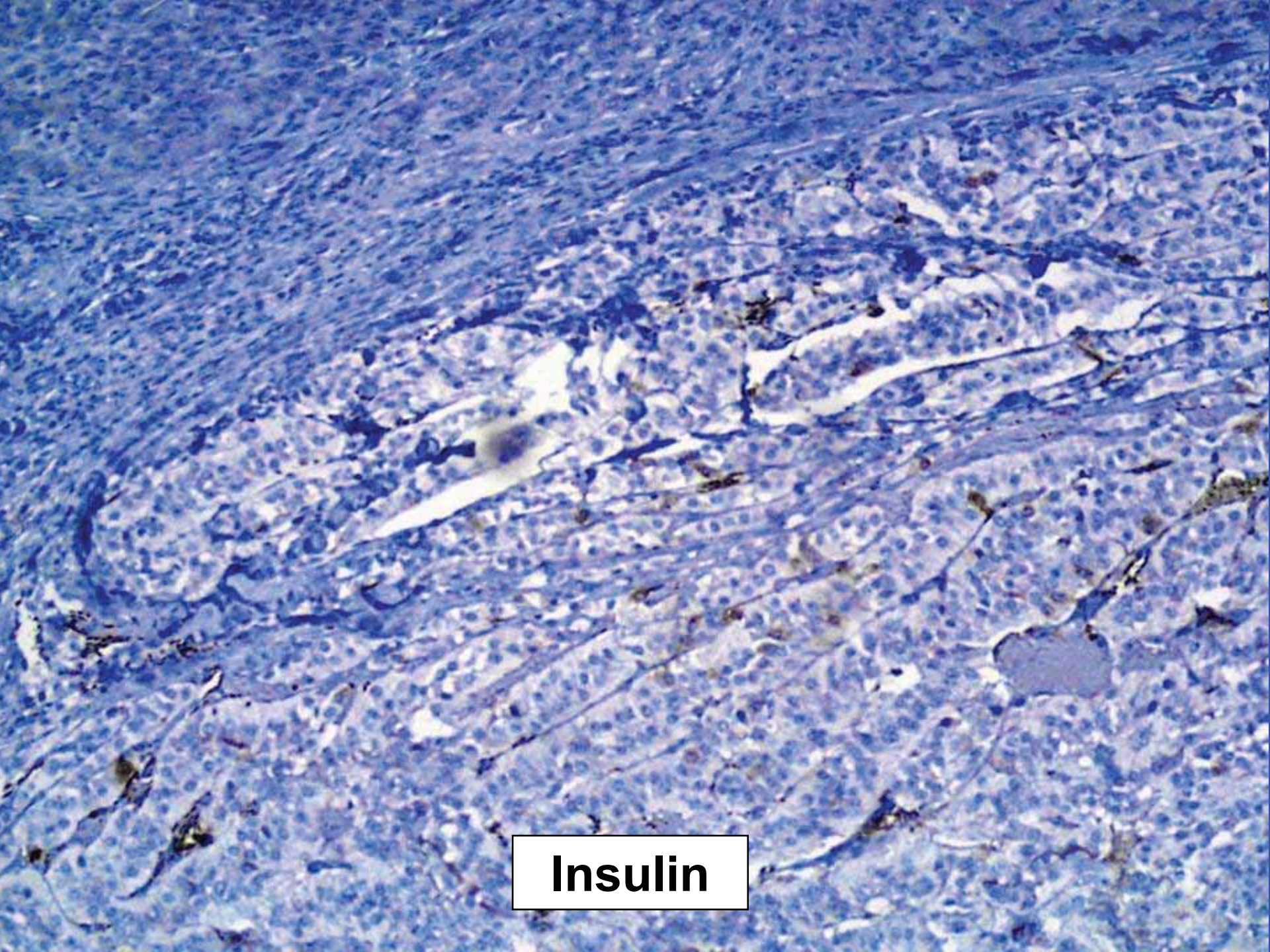




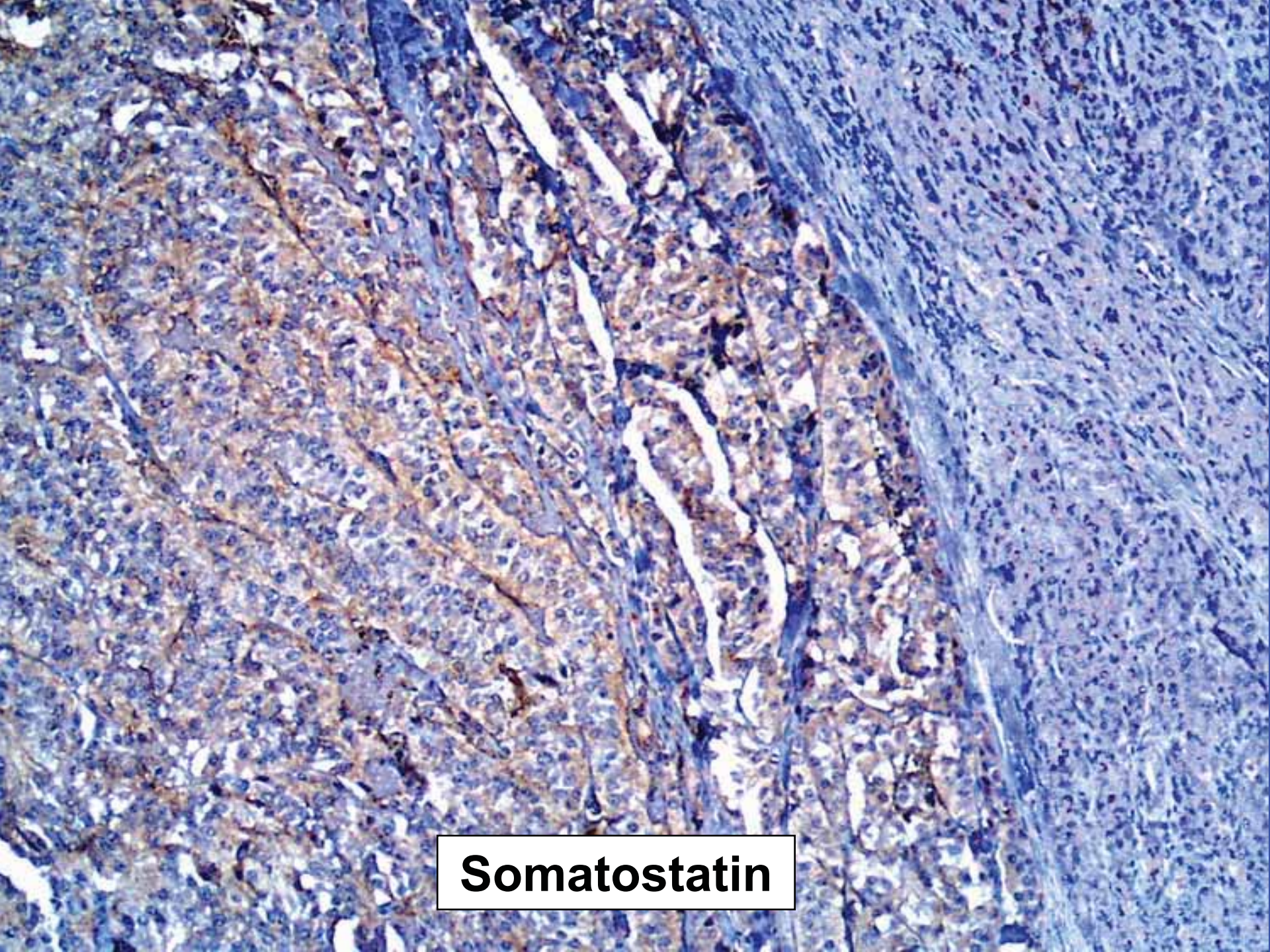
Synaptophysin



Chromogranin A+B



Insulin



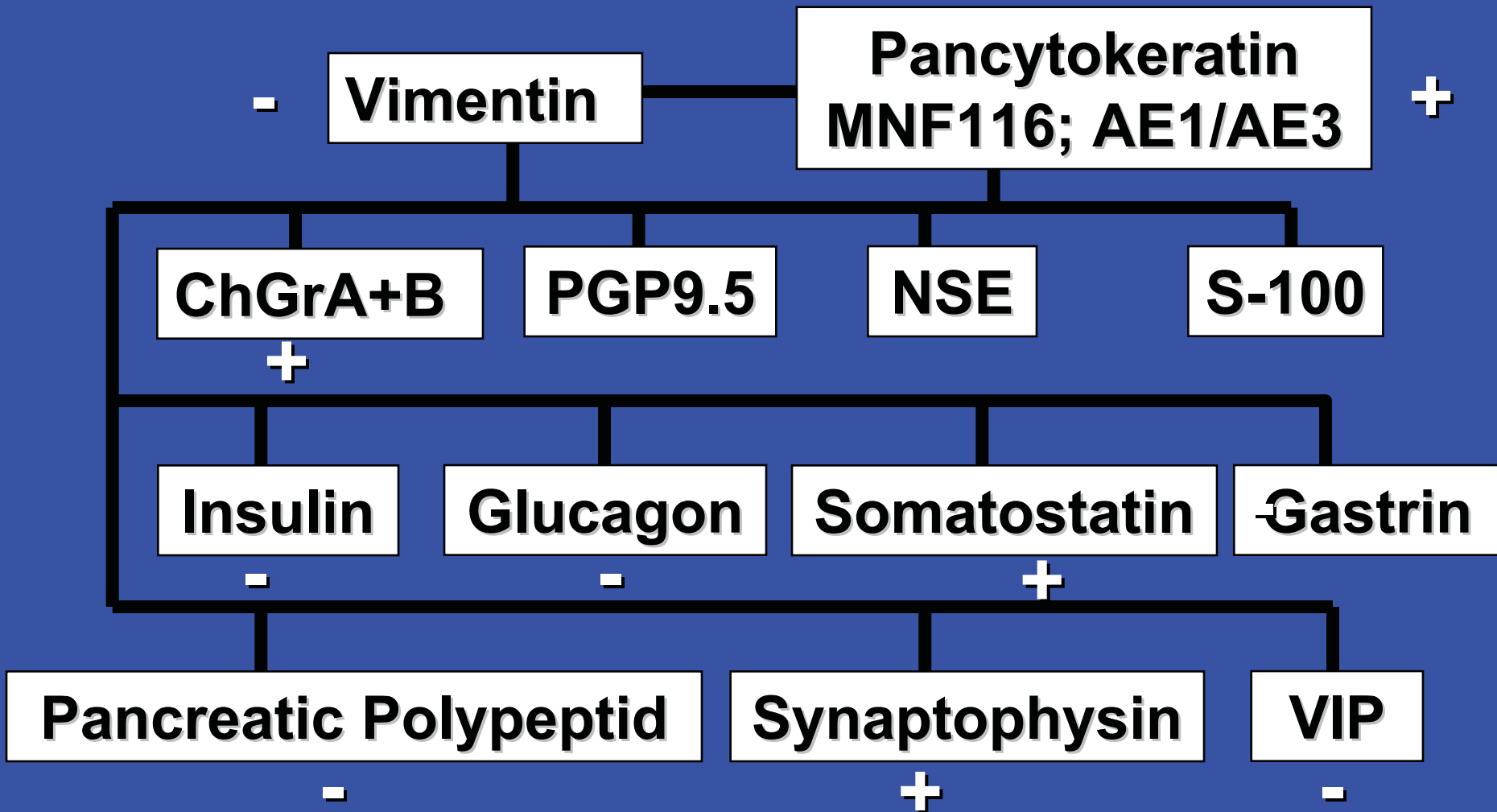
Somatostatin

What's your Diagnosis



"I said SIT!, You Idiot!"

Somatostatinoma



Pituitary Gland

- **Anatomy: anterior (adenohypophysis) and posterior (neurohypophysis)**
- **Adenohypophysis: pars distalis, intermedia, tuberalis**
- **Pars distalis: 5 cell types that produce hormones:**
 - **somatotrophs (lateral wings): growth hormones**
 - **lactotrophs (random, posterolateral): prolactin**
 - **corticotrophs (central, lateral): ACTH, MSH, ED**
 - **thyrotrophs (anteromedial): TSH**
 - **gonadotrophs (random): FSH and LH**
- **Pars intermedia: - mainly corticotrophs: POMC**
- **Pars tuberalis: - mainly gonadotrophs: FSH, LH**

Classification of Pituitary Tumors

GH-PRL-TSH Family

GH-containing somatotroph adenomas/carcinomas

Densely granulated somatotroph adenomas/carcinomas

Sparsely granulated somatotroph adenomas/carcinomas

GH- and PRL-containing mammosomatotroph adenomas/carcinomas

PRL-containing lactotroph adenomas/carcinomas

Sparsely granulated lactotroph adenomas/carcinomas

Densely granulated lactotroph adenomas/carcinomas

PRL-cell adenomas/carcinomas with GH content (acidophil stem cell)

TSH-containing thyrotroph adenomas/carcinomas

GH-, PRL-, and TSH-containing adenomas/carcinomas

ACTH Family

ACTH-containing corticotroph adenomas/carcinomas

Densely granulated corticotroph adenomas/carcinomas

Sparsely granulated corticotroph adenomas/carcinomas

Gonadotropin Family

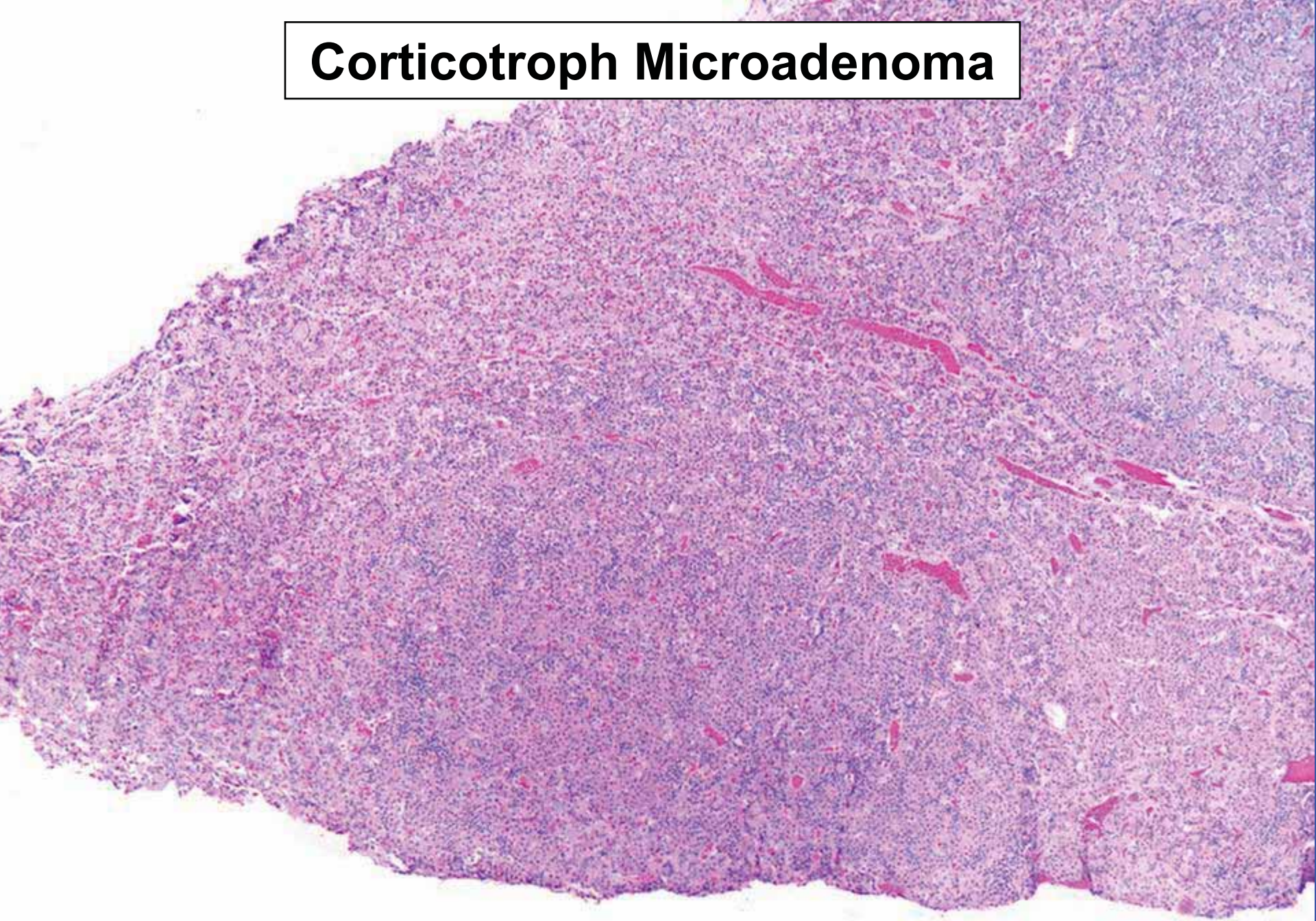
FSH/LH-containing gonadotroph adenomas/carcinomas

Unclassified adenomas/carcinomas

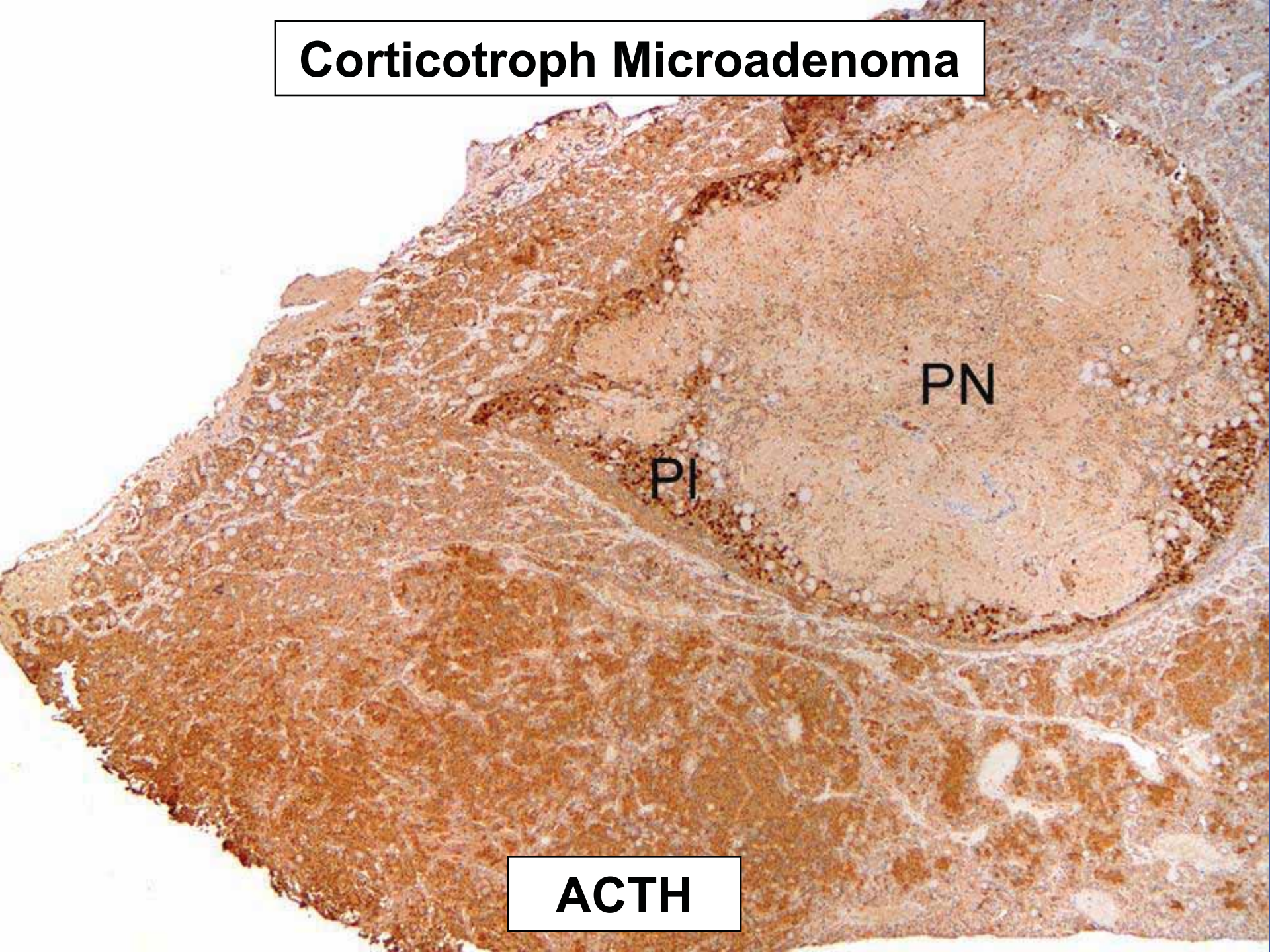
Unusual plurihormonal adenomas/carcinomas

Immunonegative adenomas/carcinomas

Corticotroph Microadenoma



Corticotroph Microadenoma



PN

PI

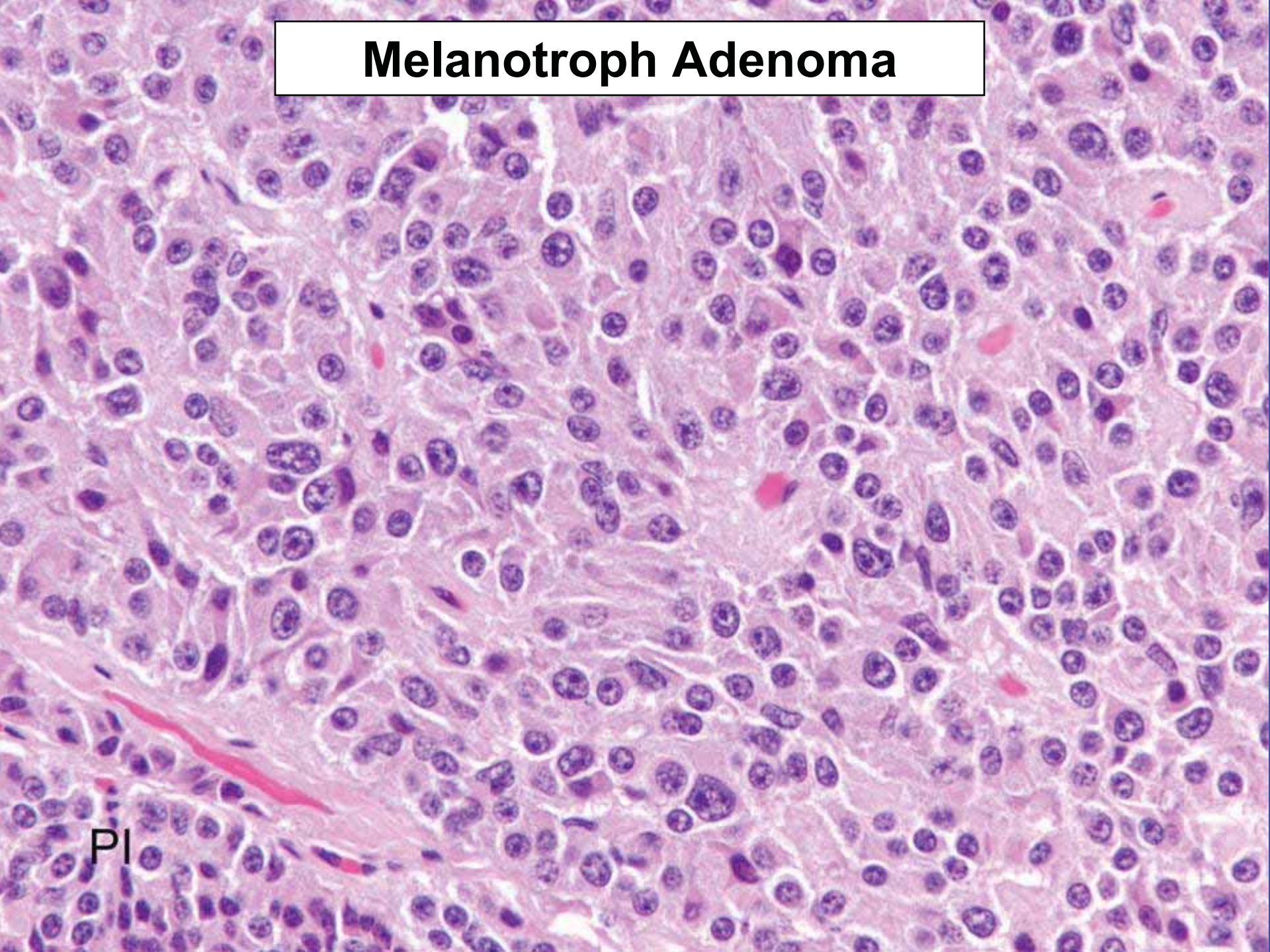
ACTH

Somatotroph Adenoma



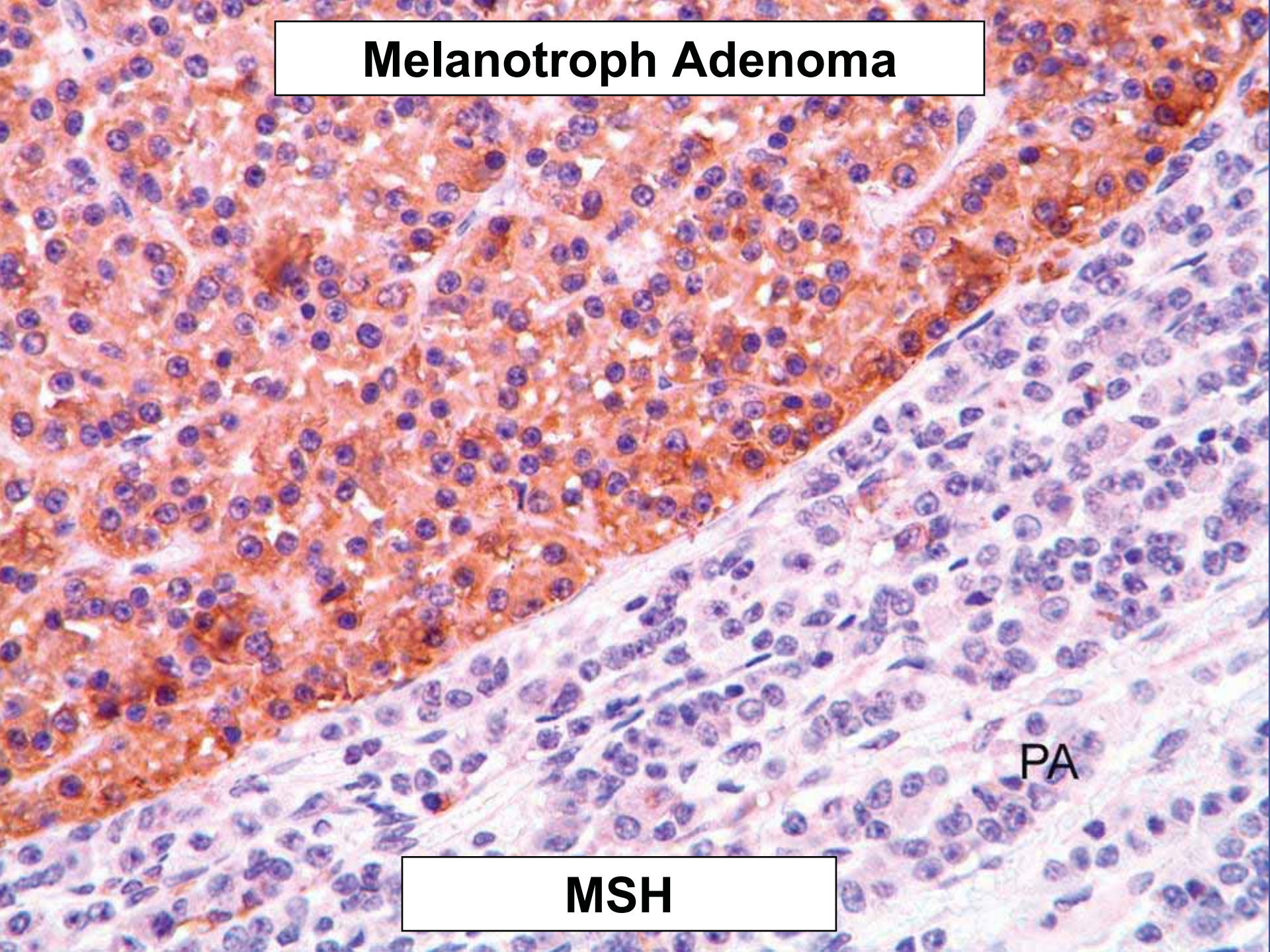
Growth Hormone

Melanotroph Adenoma



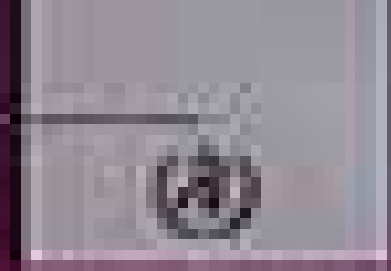
PI

Melanotroph Adenoma



PA

MSH



**Histological
Classification
of
Tumors of the
Endocrine System
of Domestic Animals**



**Histological Classification of
Tumors of the Endocrine System
of Domestic Animals**

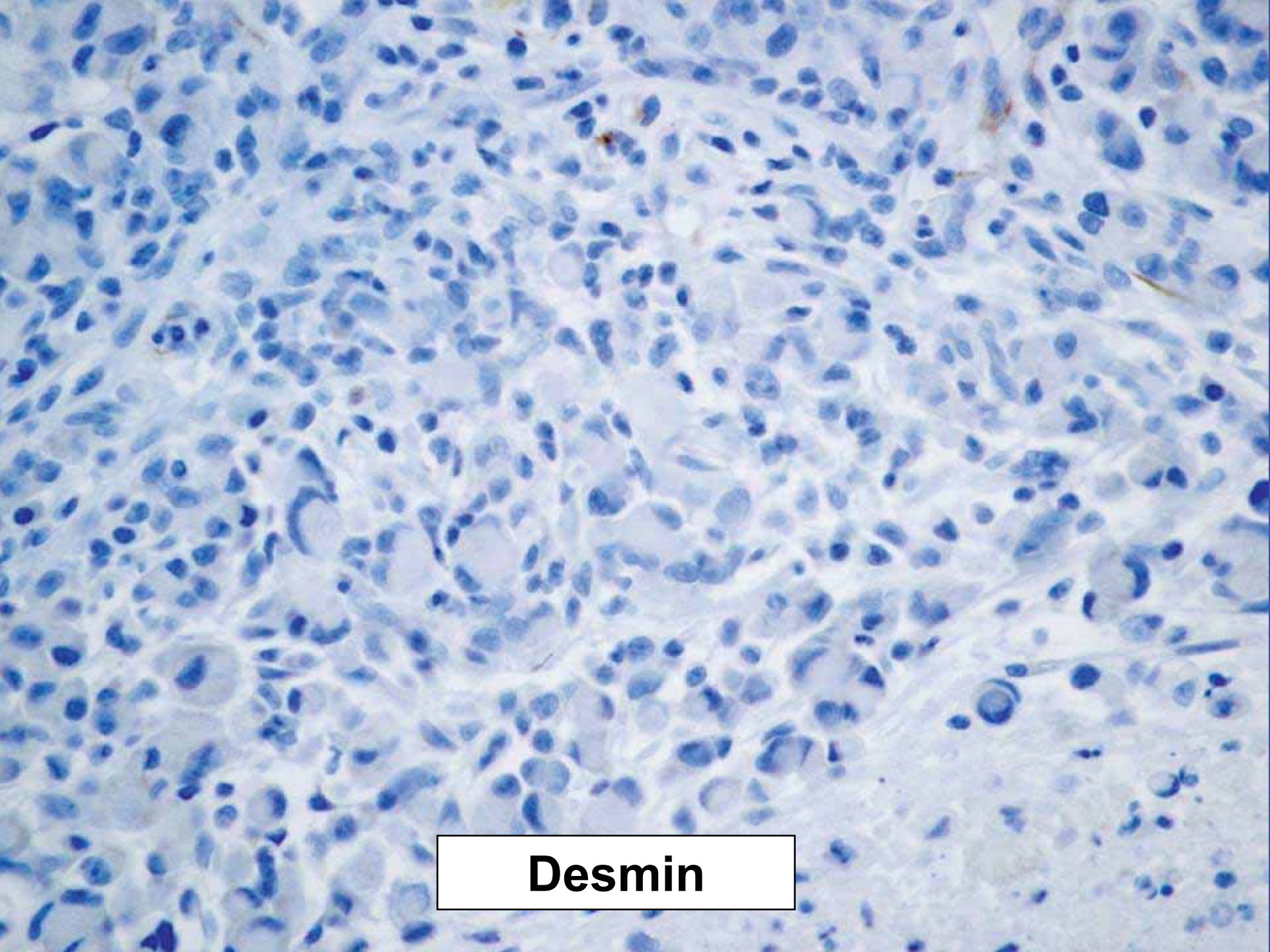
**Authors: M. Kiupel, C. Capen, M.
Miller, R. Smedley.**

ISBN: 978-1-4276-3153-4

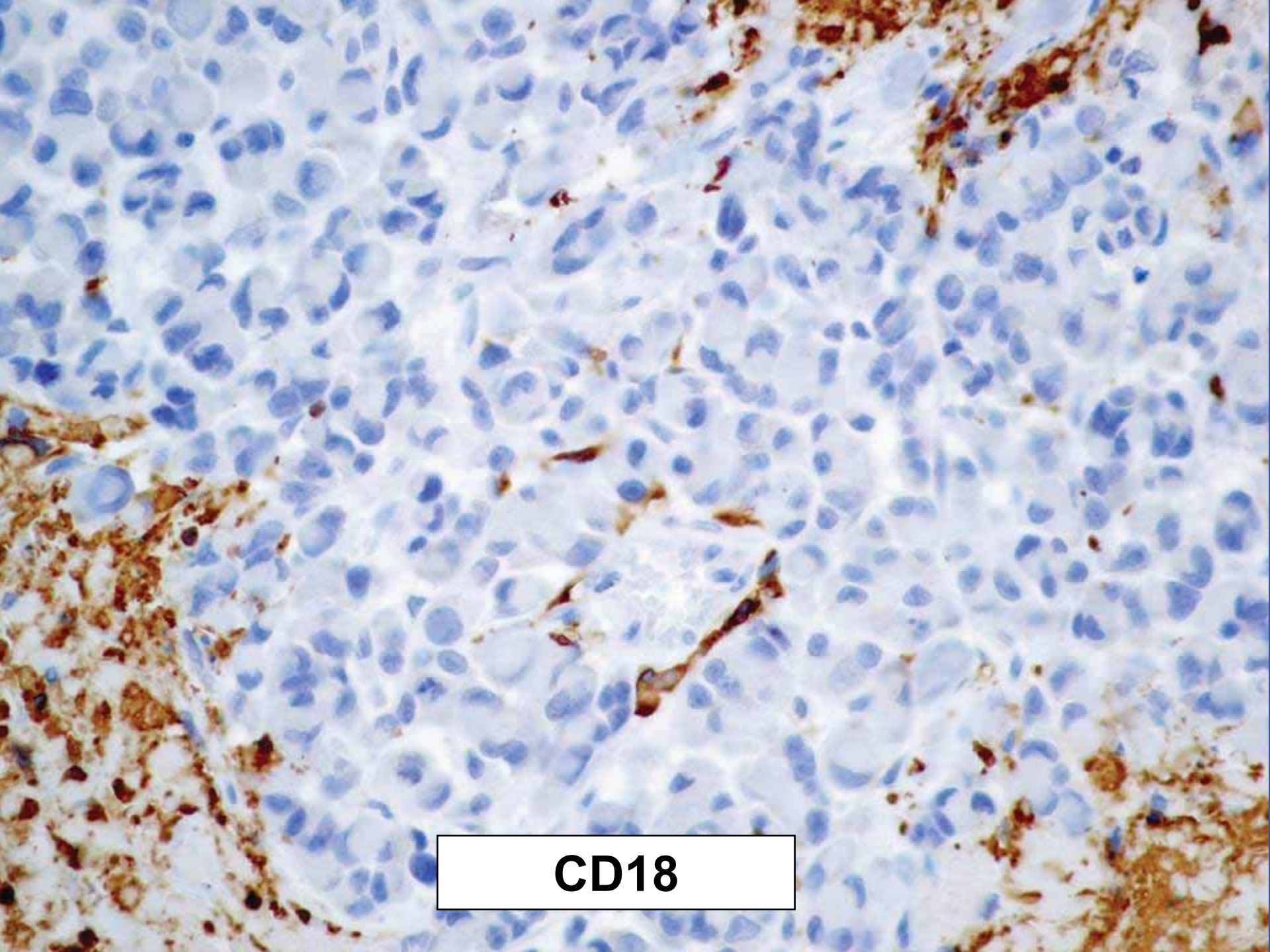
List Price \$70.00

Sublingual Mass

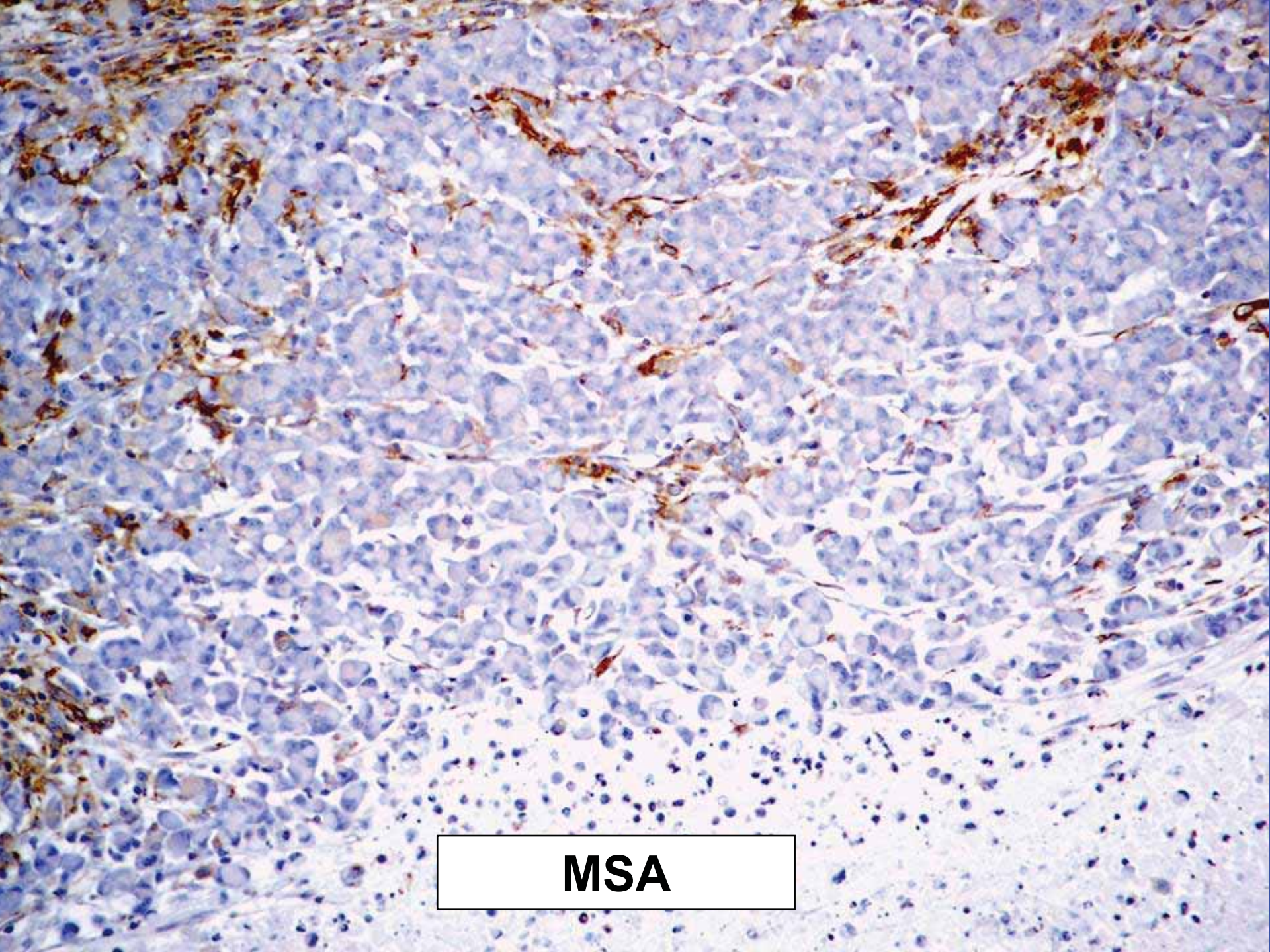




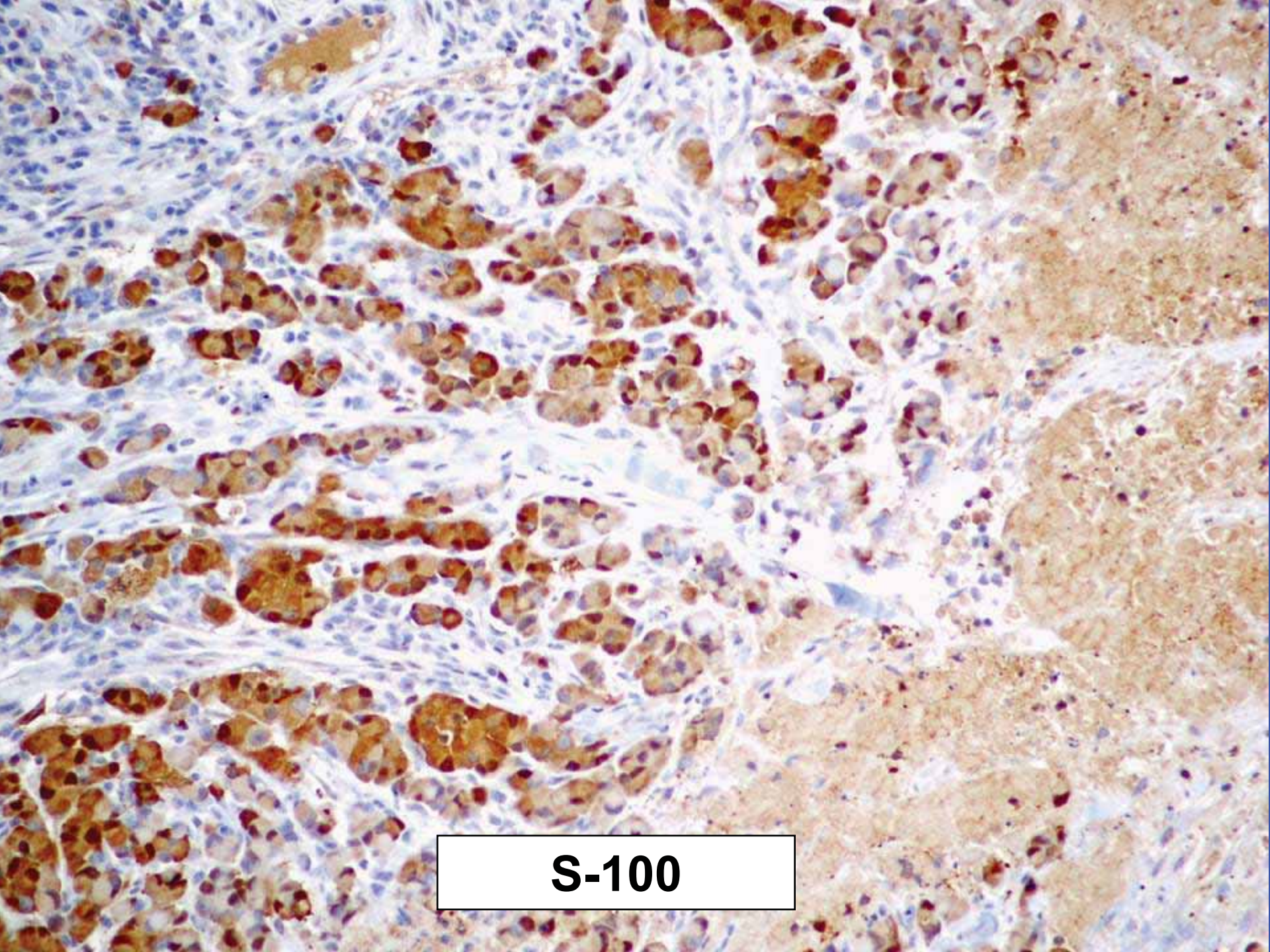
Desmin



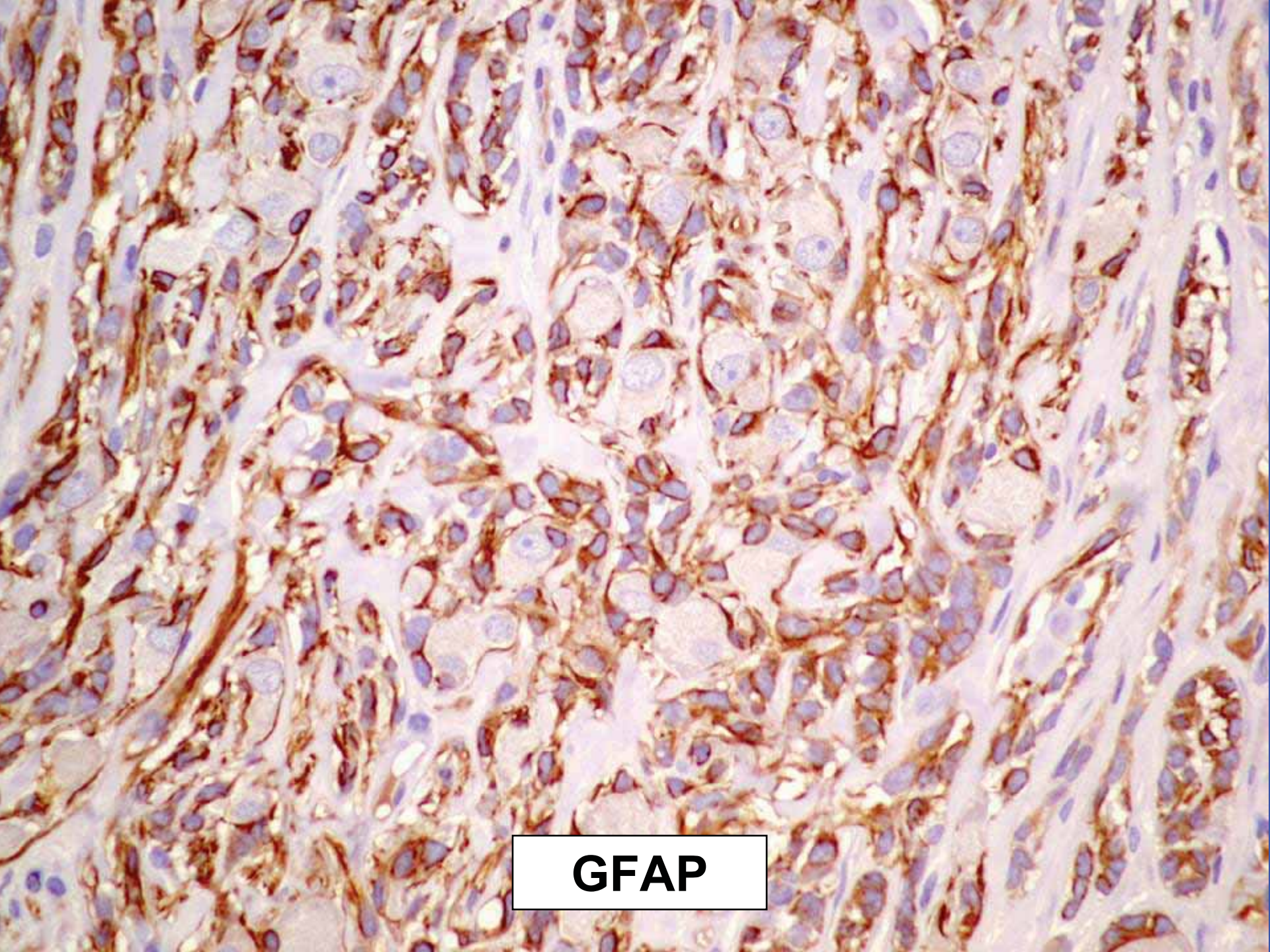
CD18



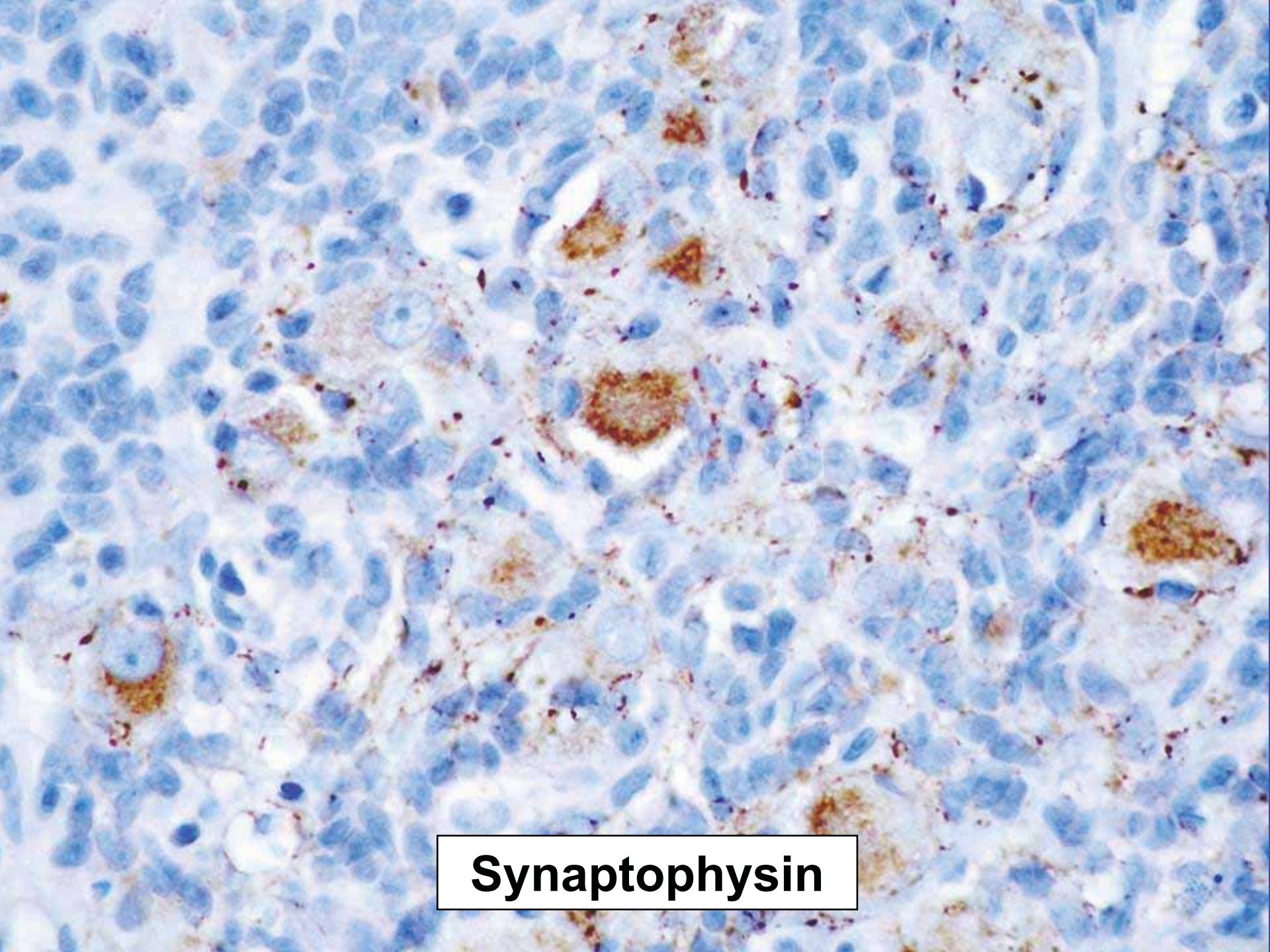
MSA



S-100



GFAP

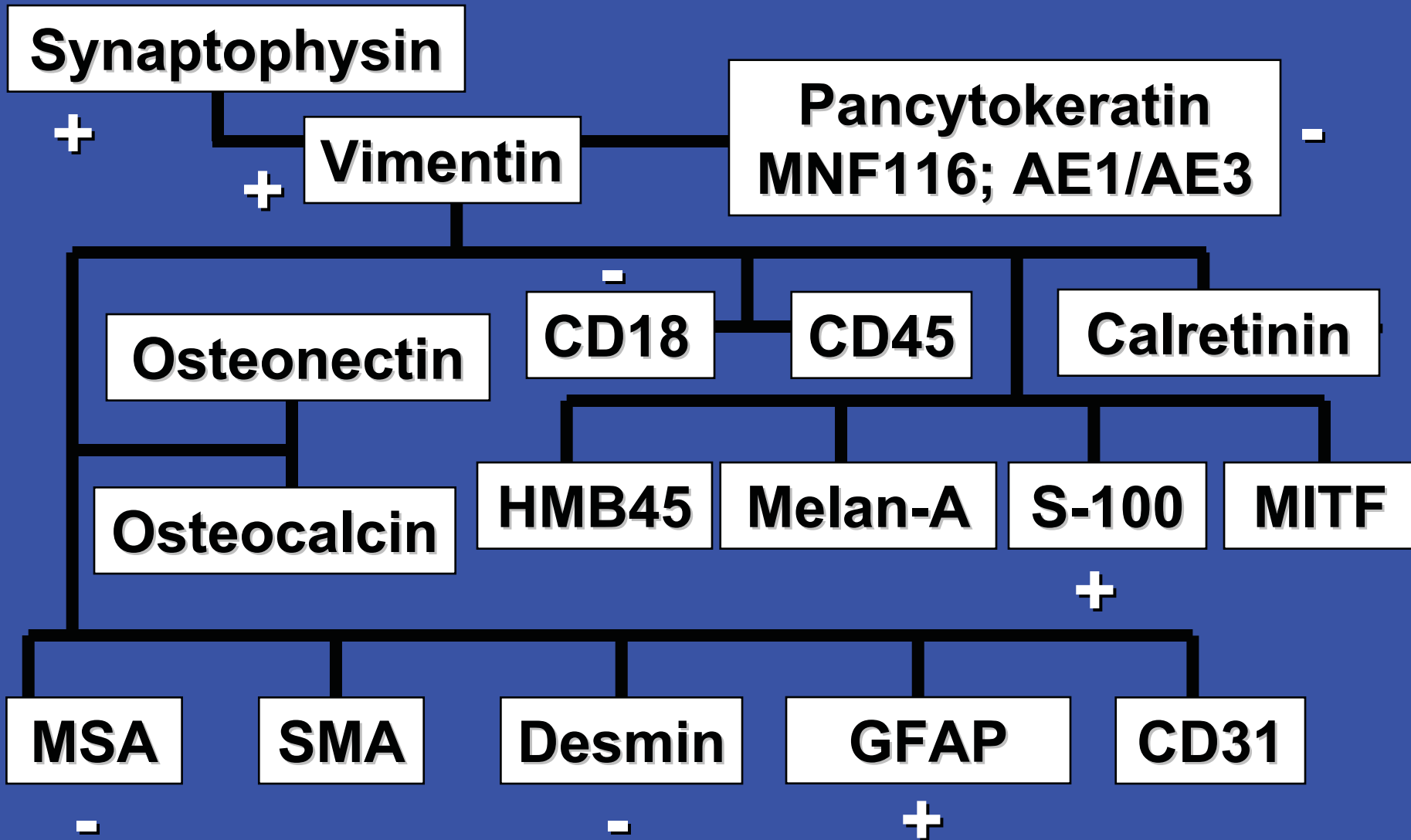


Synaptophysin

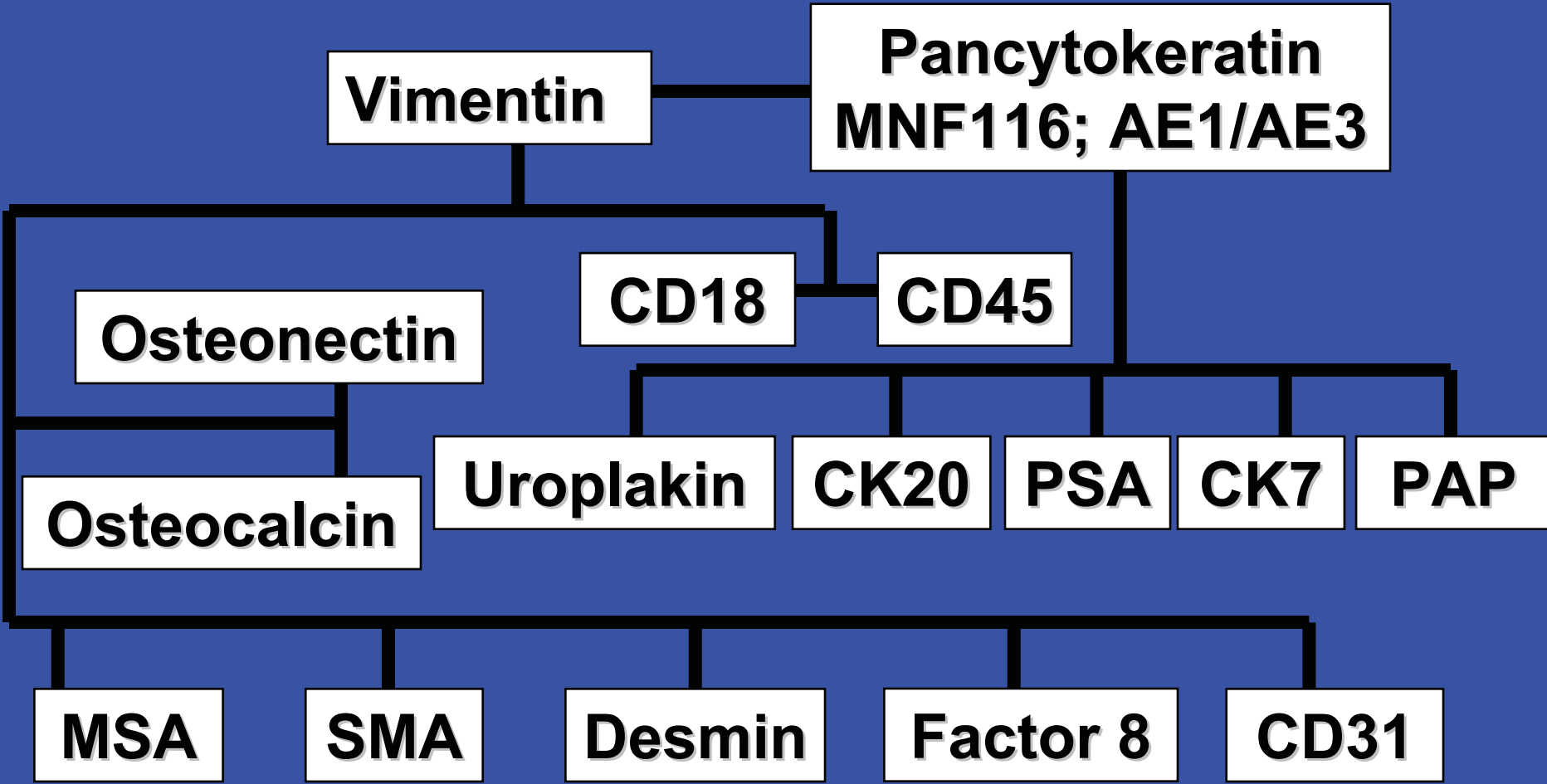
What's your Diagnosis



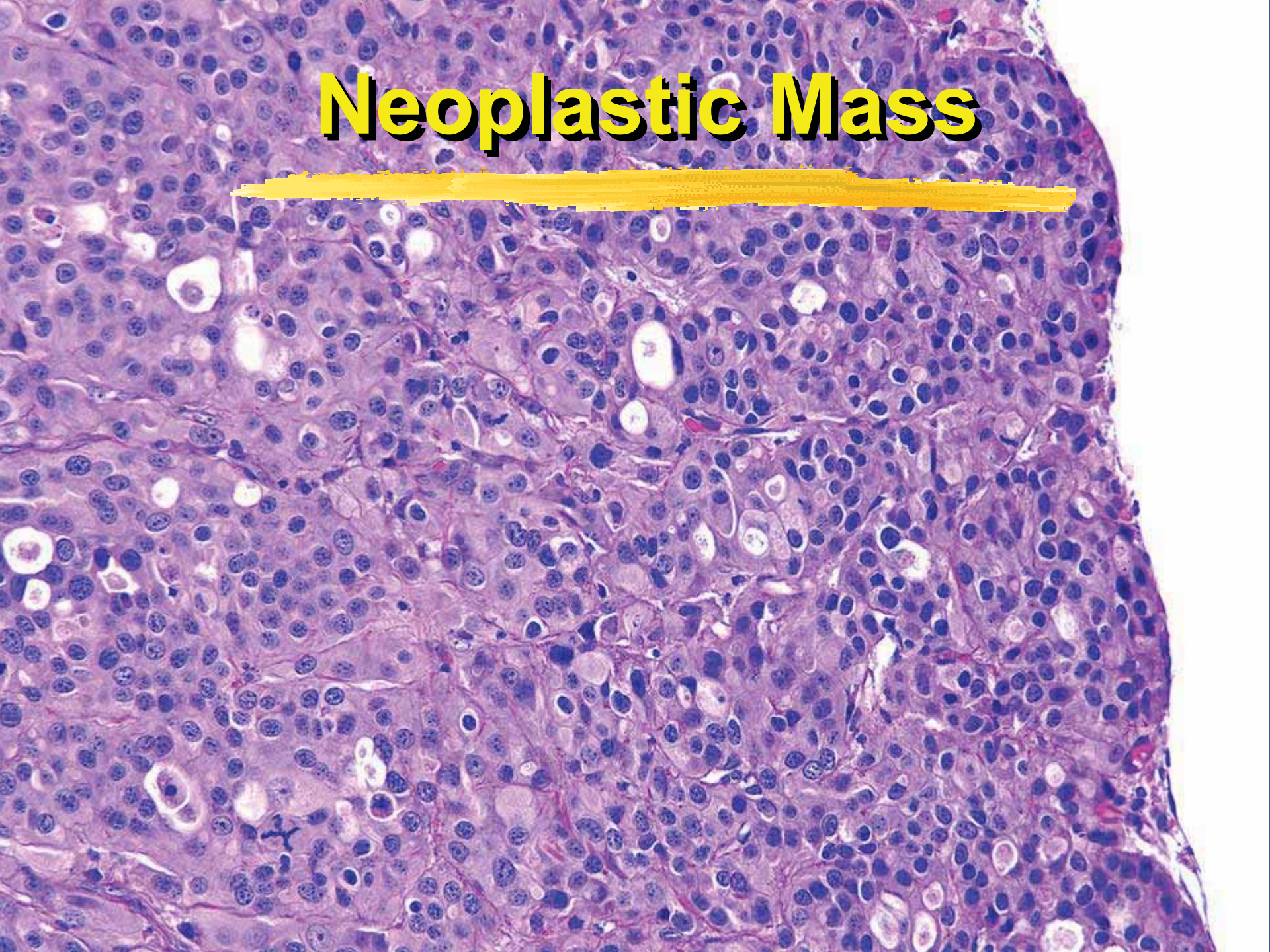
Ganglioneuroma

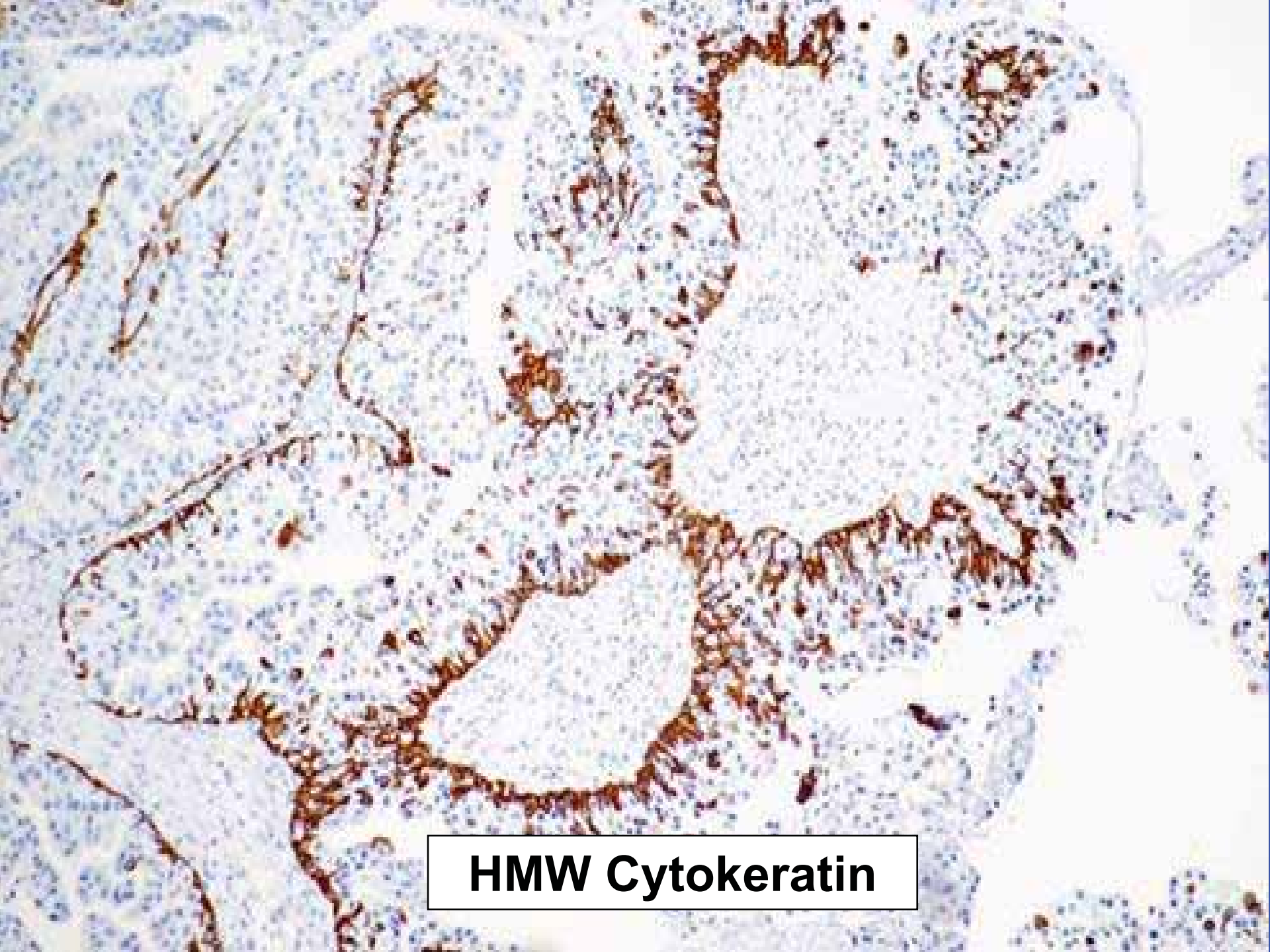


Tumors of the Urogenital Tract

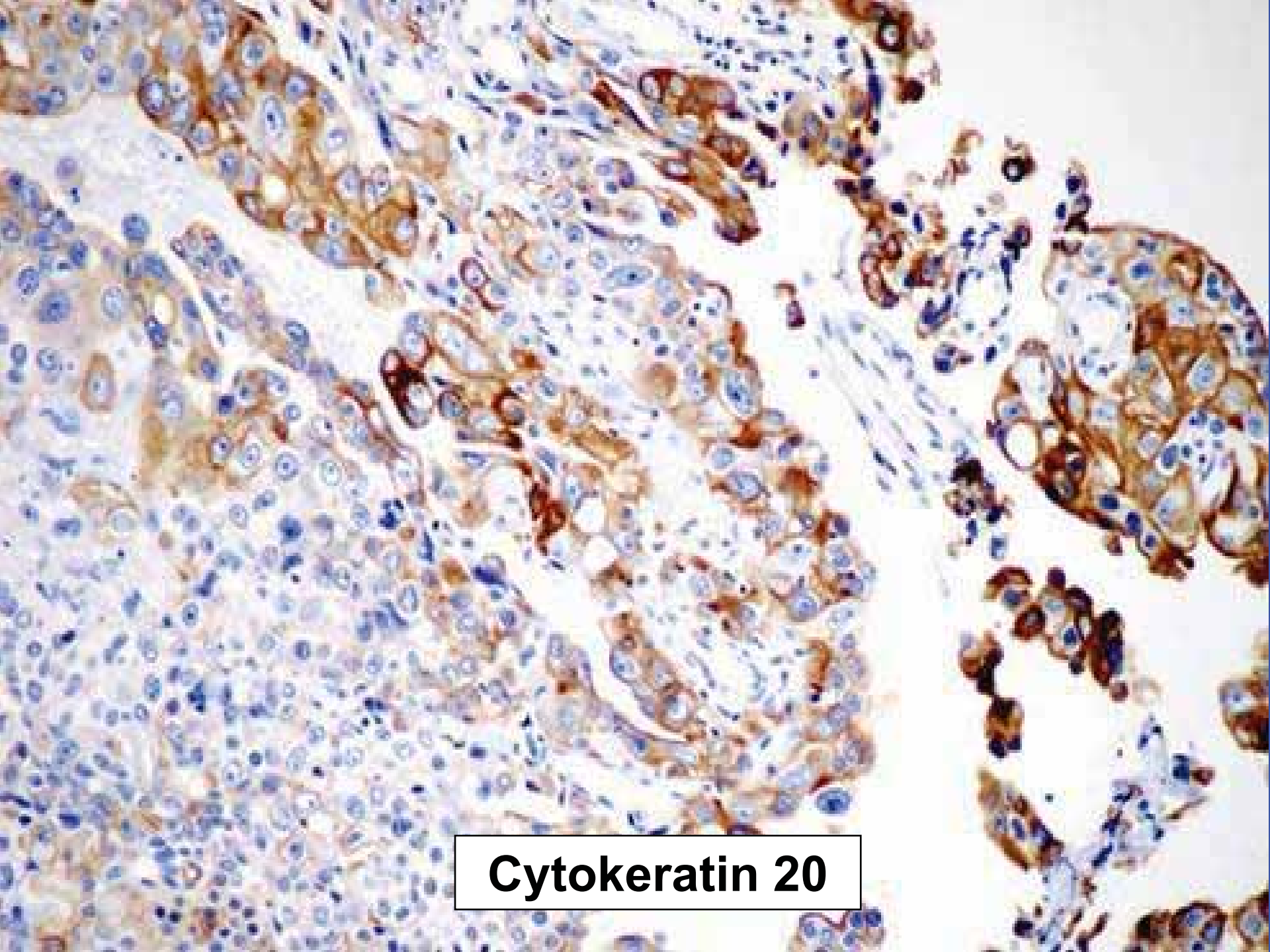


Neoplastic Mass

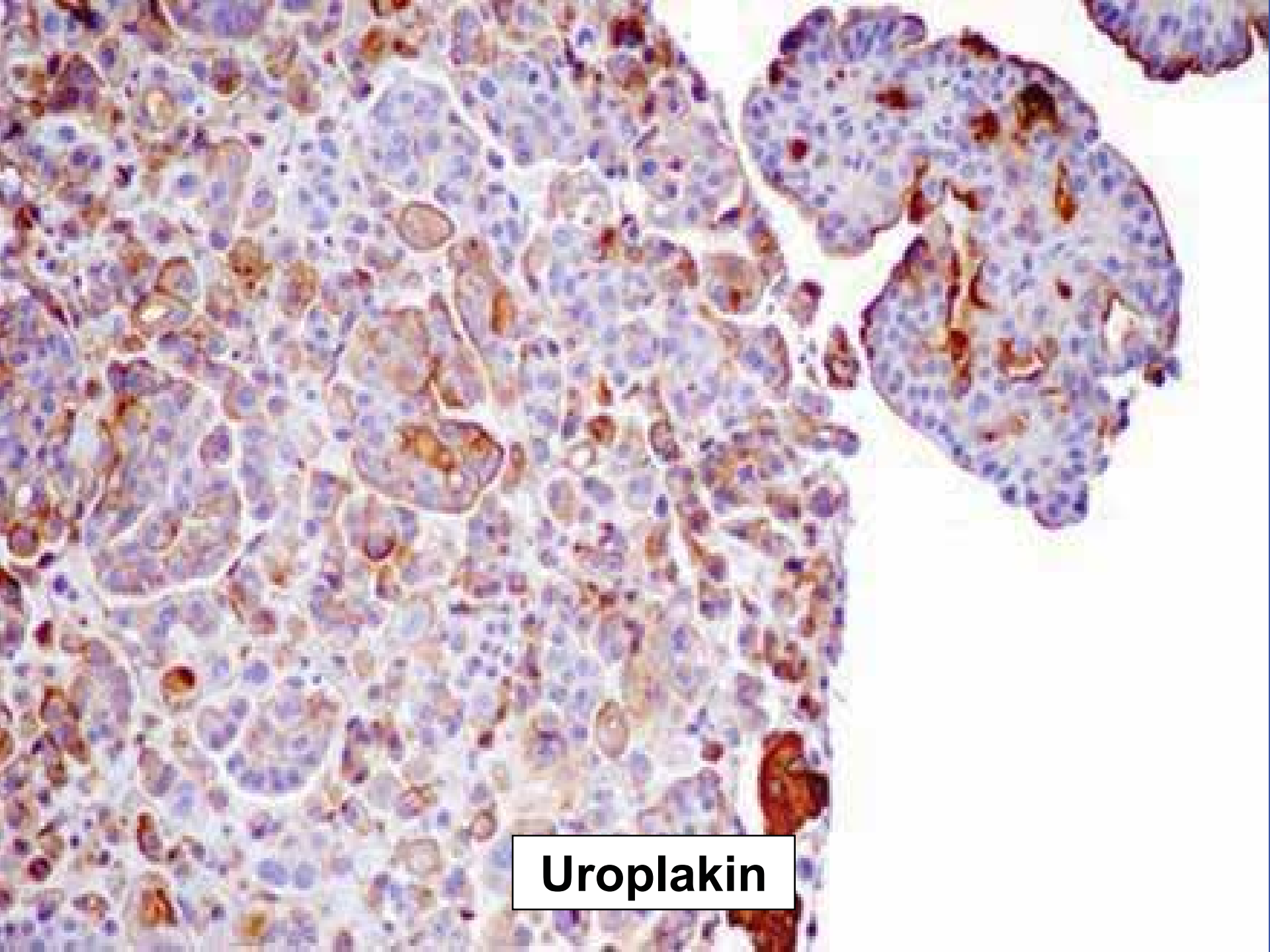





HMW Cytokeratin



Cytokeratin 20

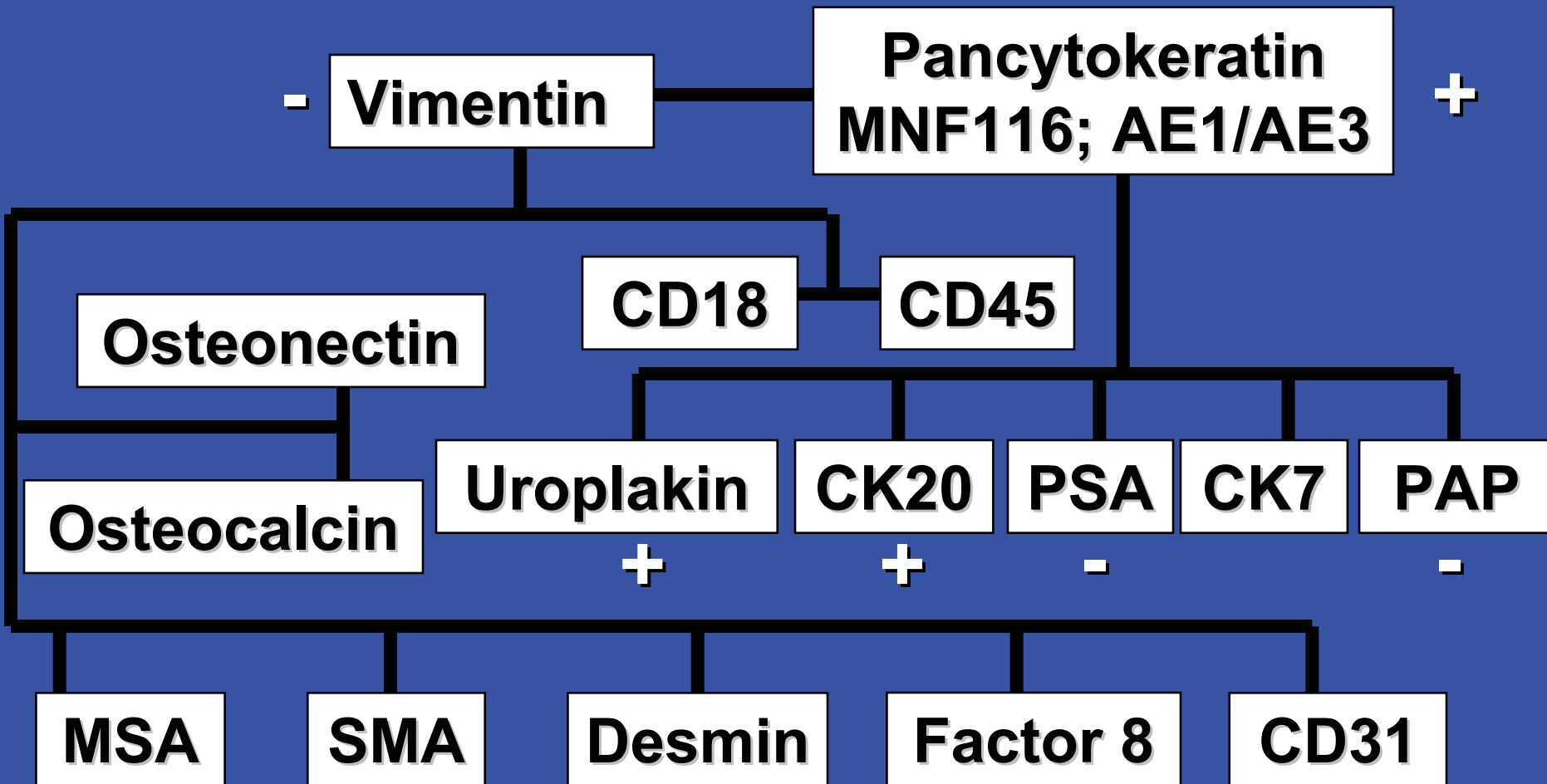


Uroplakin

A photograph of a rural farm scene. In the background, there is a red barn with a white roof. In the foreground, a large black silo stands prominently. The ground is covered in green grass, and there are some trees and utility poles in the distance. The text "What's your Diagnosis" is overlaid in the bottom left corner in a bold, yellow font with a black outline.

**What's your
Diagnosis**

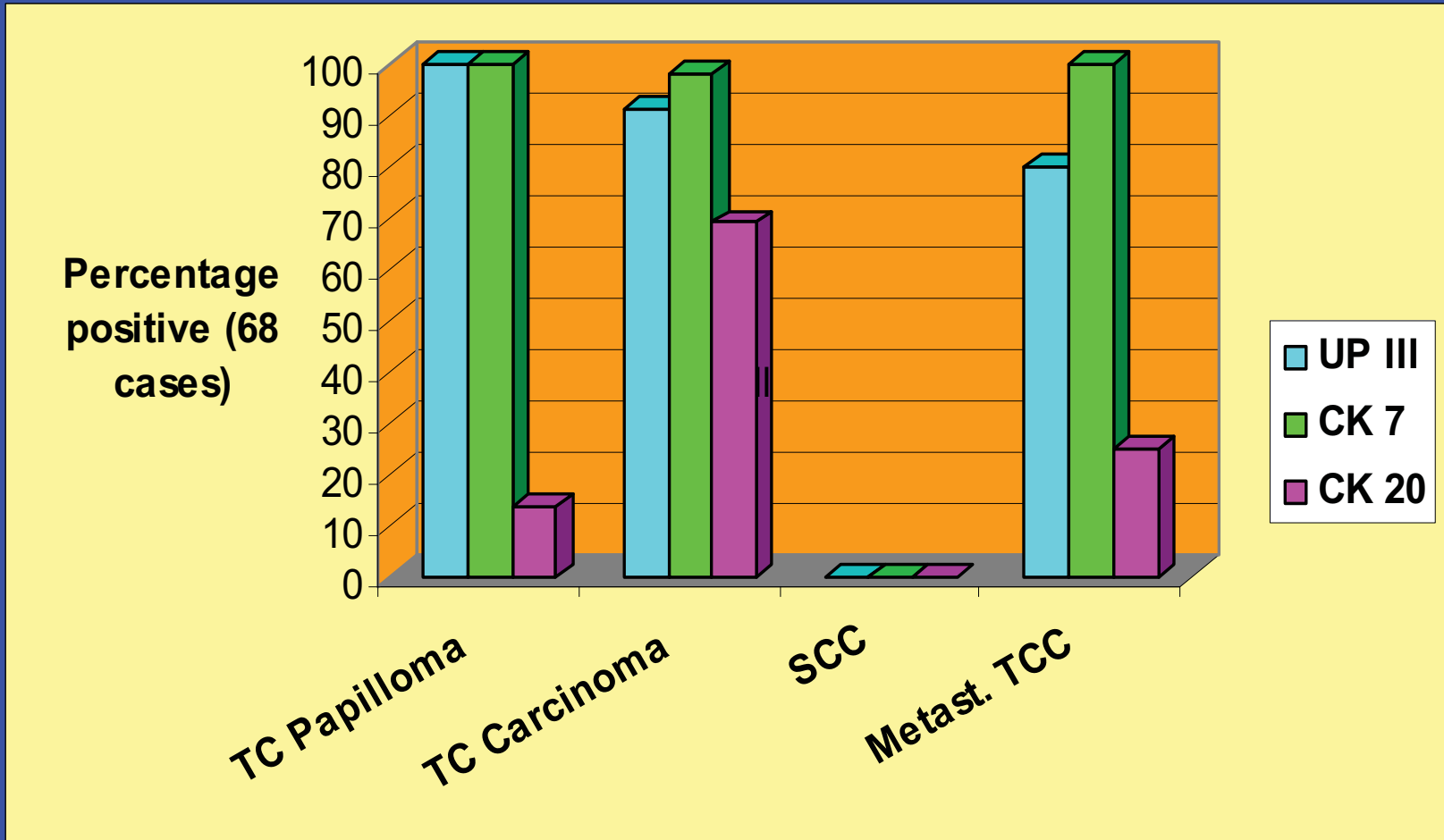
Transitional Cell Carcinoma



Canine Urothelial Tumors

- **Cytokeratins**
 - Low molecular weight CKs: 7, 8, 18, 19, 20
 - High molecular weight CKs: 13, 17
- **Uroplakin**
 - Majority of urothelial tumors (papillomas and transitional cell carcinomas) are positive for UP III
 - Staining is membranous and cytoplasmic
 - Intracytoplasmic vacuoles are positive
 - Metastases are positive (80%)
- CK 7 is more sensitive but less specific than UP III

Expression of UP III, CK 7 & CK 20 in Canine Urothelial Tumors

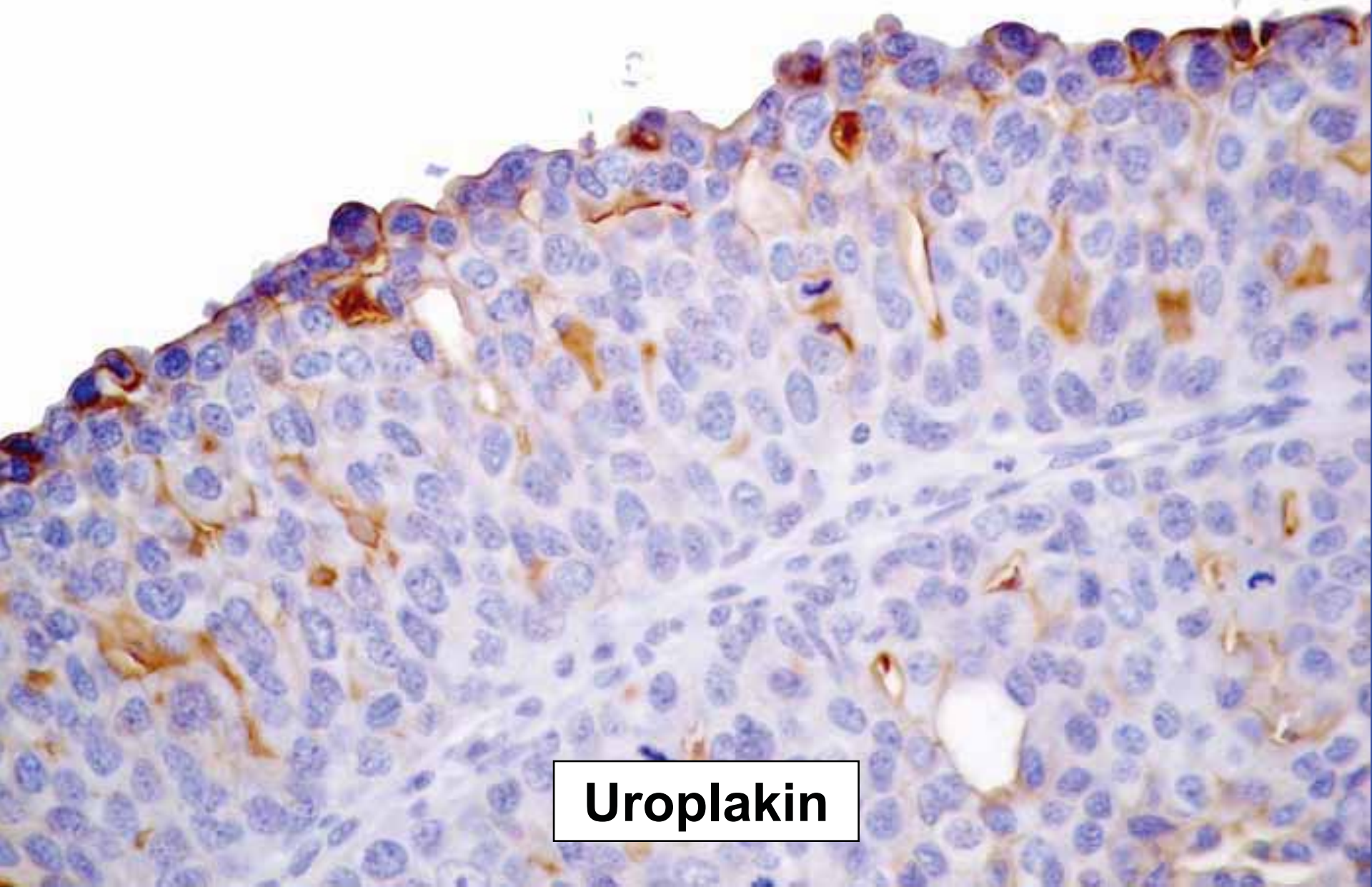


A histological section of bladder tissue stained with hematoxylin and eosin (H&E). The image shows a cross-section of the bladder wall, including the mucosa, submucosa, and muscularis. The mucosal layer is characterized by a thick, multi-layered epithelium. The surface of the epithelium is covered by a layer of urothelial cells, which are stained brown. The underlying layers consist of numerous cells with blue nuclei and pink cytoplasm/extracellular matrix. The overall structure is highly organized and shows typical features of bladder tissue.

Bladder

Uroplakin

Grade 1 TCC



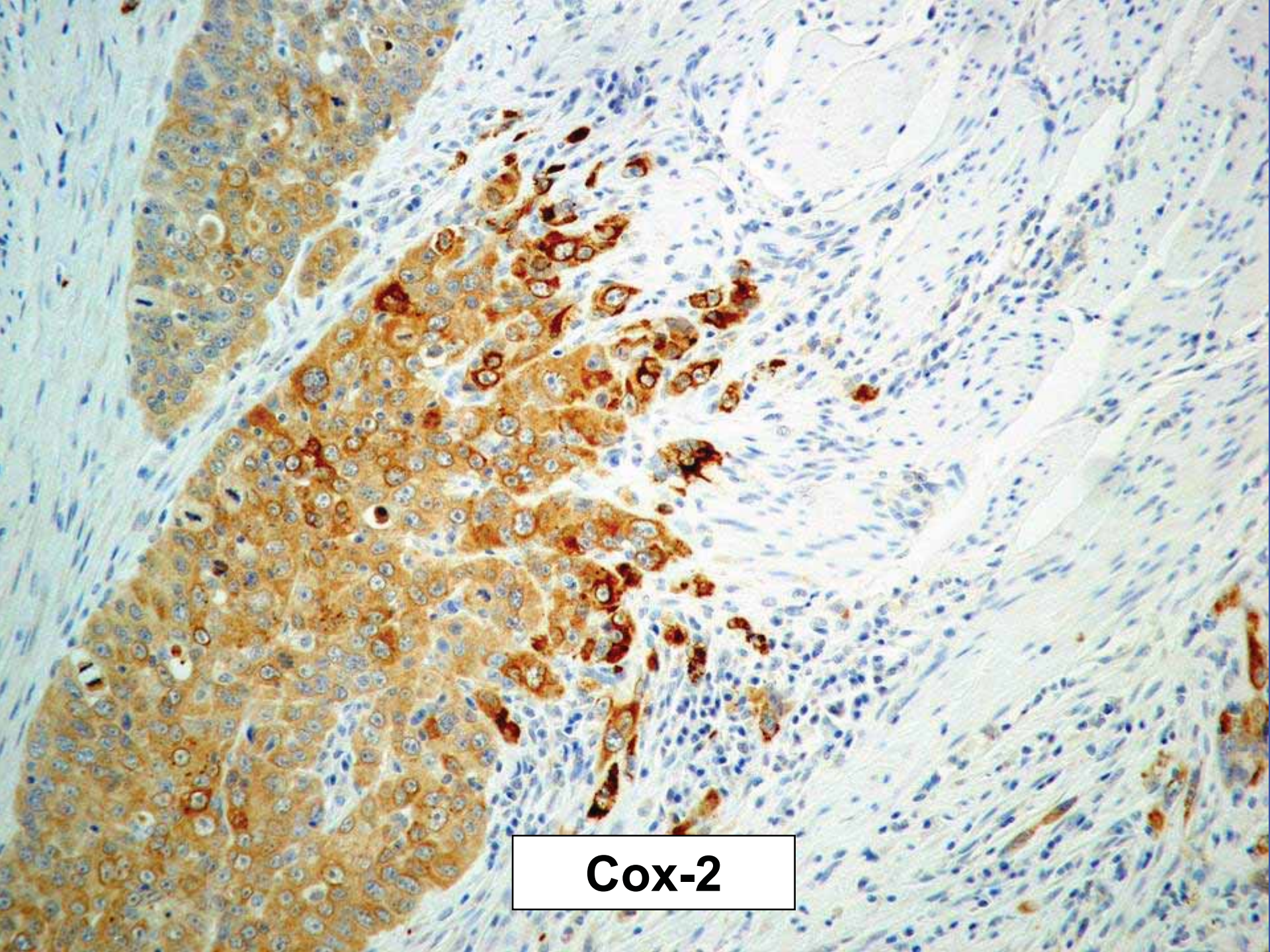
Uroplakin



Grade 3 TCC

This histological slide shows a section of bladder tissue with a high-grade transitional cell carcinoma. The tumor is characterized by a thick, multi-layered epithelium with significant cellular atypia, including enlarged, hyperchromatic nuclei and a loss of normal cellular polarity. The cells are arranged in a disorganized, papillary pattern. The staining highlights the presence of uroplakin, a marker for transitional cell carcinoma, which is visible as brownish cytoplasmic and membrane staining in the tumor cells. The surrounding stroma shows a dense infiltrate of inflammatory cells.

Uroplakin



Cox-2



A histological section of bladder tissue stained with hematoxylin and eosin (H&E). The tissue shows a thick, multi-layered epithelium with numerous nuclei stained blue. A prominent, dark brown, wavy line of staining is visible along the right edge of the tissue, indicating the presence of PGDH. The overall structure is dense and cellular.

Bladder

PGDH



Invasive TCC

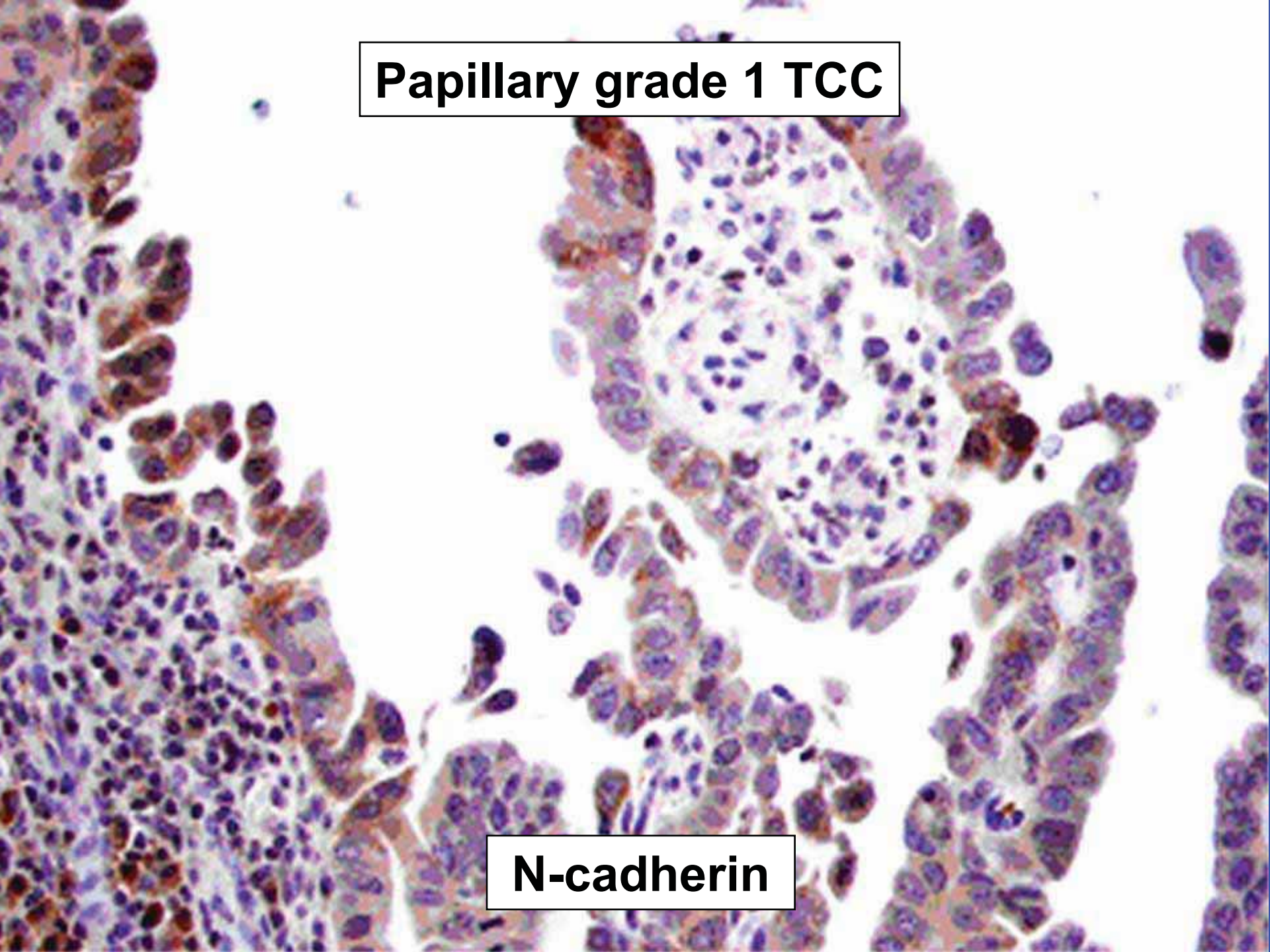
This histological image shows a section of bladder tissue. The left side of the image displays a thick, dark purple-stained layer, which is the transitional epithelium. The right side shows a lighter, more cellular area representing the underlying connective tissue. The overall appearance is consistent with a high-grade, invasive transitional cell carcinoma (TCC) of the bladder. The tumor cells are densely packed and show significant nuclear atypia and loss of normal tissue architecture.

PGDH

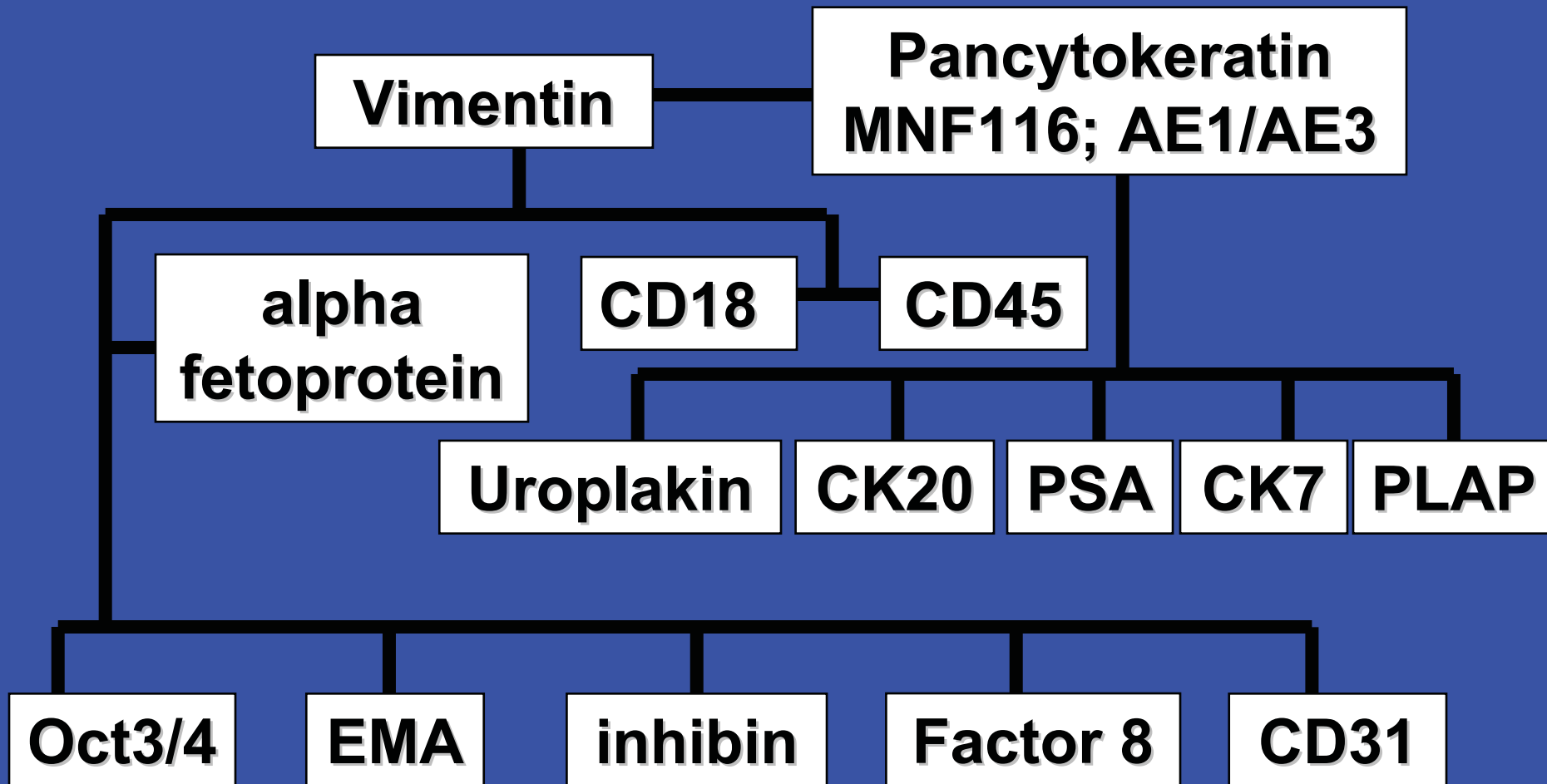
This label indicates the presence of the enzyme PGDH (Phosphoglucoisomerase) in the tissue. The enzyme is a marker for the epithelial origin of the tumor cells, and its presence is consistent with the diagnosis of transitional cell carcinoma. The staining is localized to the tumor cells, highlighting their epithelial nature.

Papillary grade 1 TCC

N-cadherin

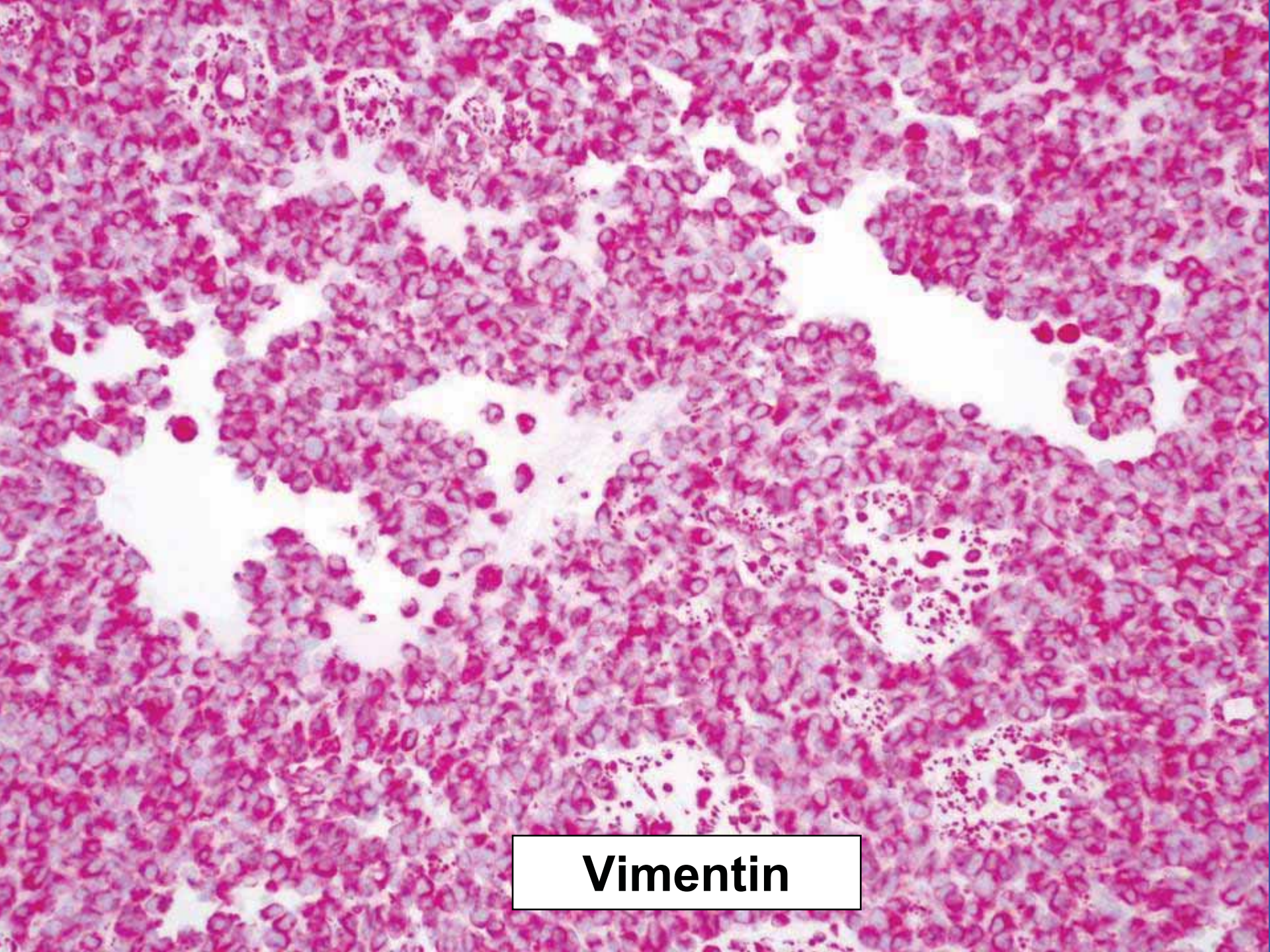


Tumors of the Genital Tract

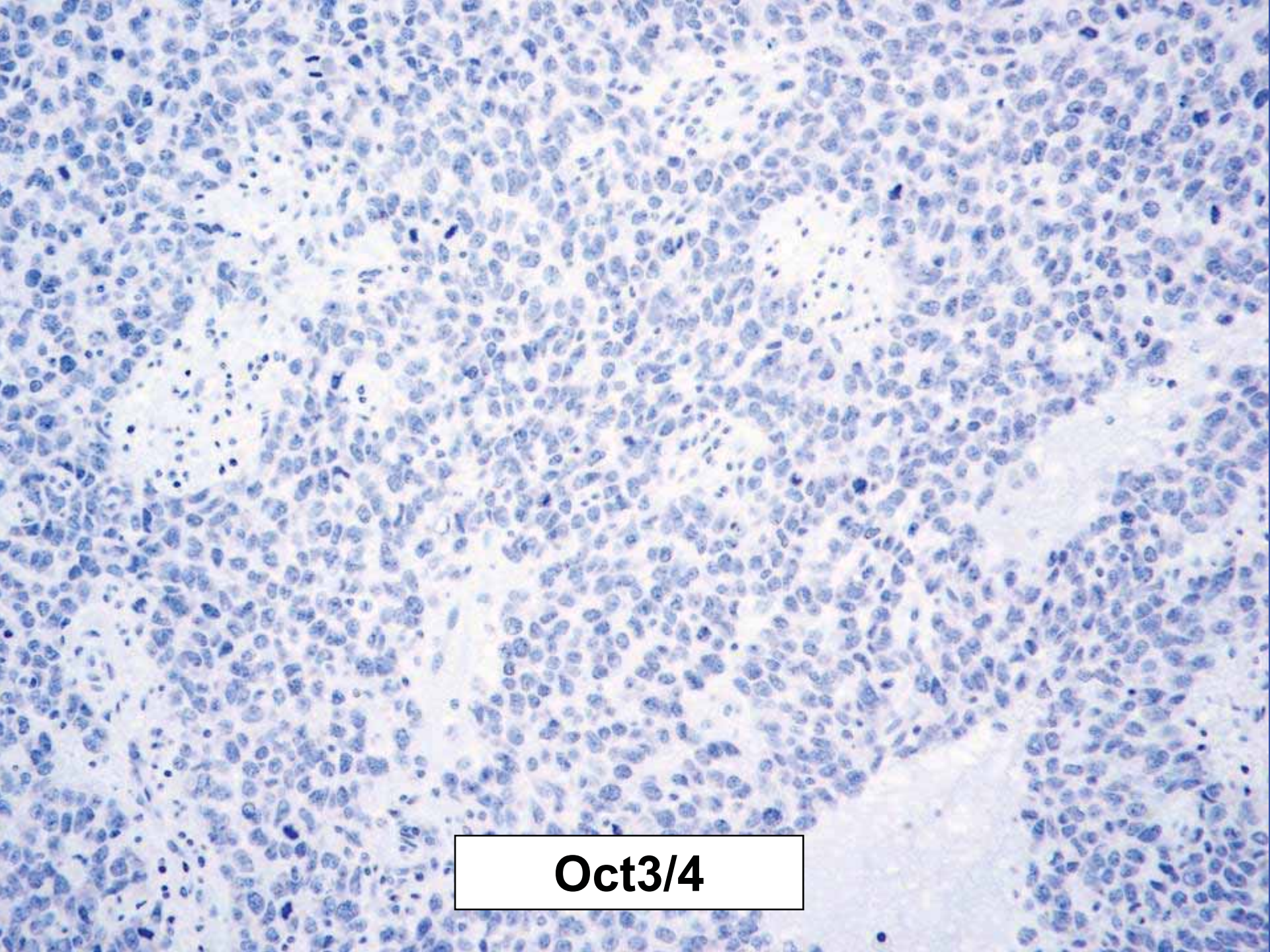


Neoplastic Mass

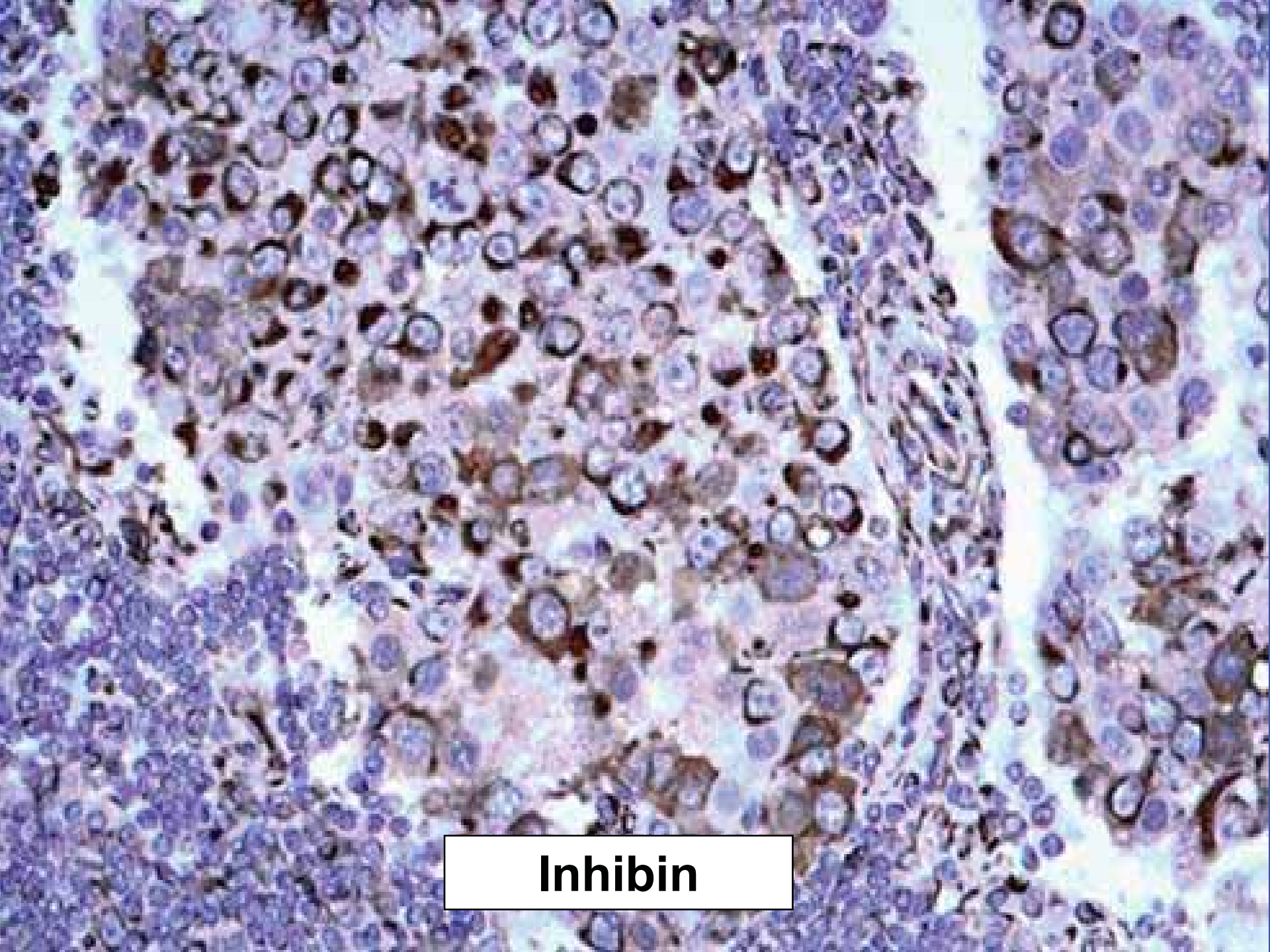





Vimentin



Oct3/4

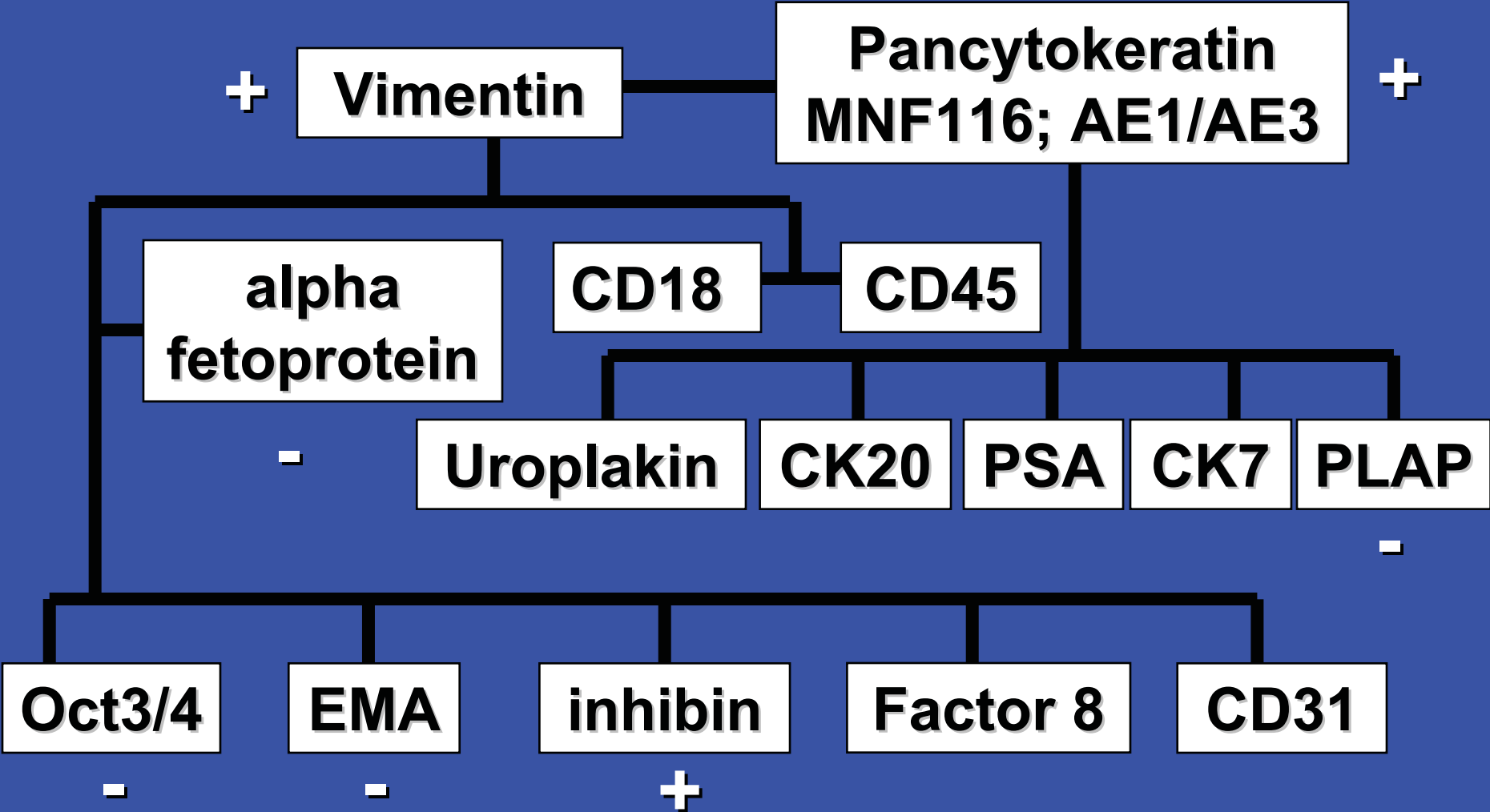


Inhibin

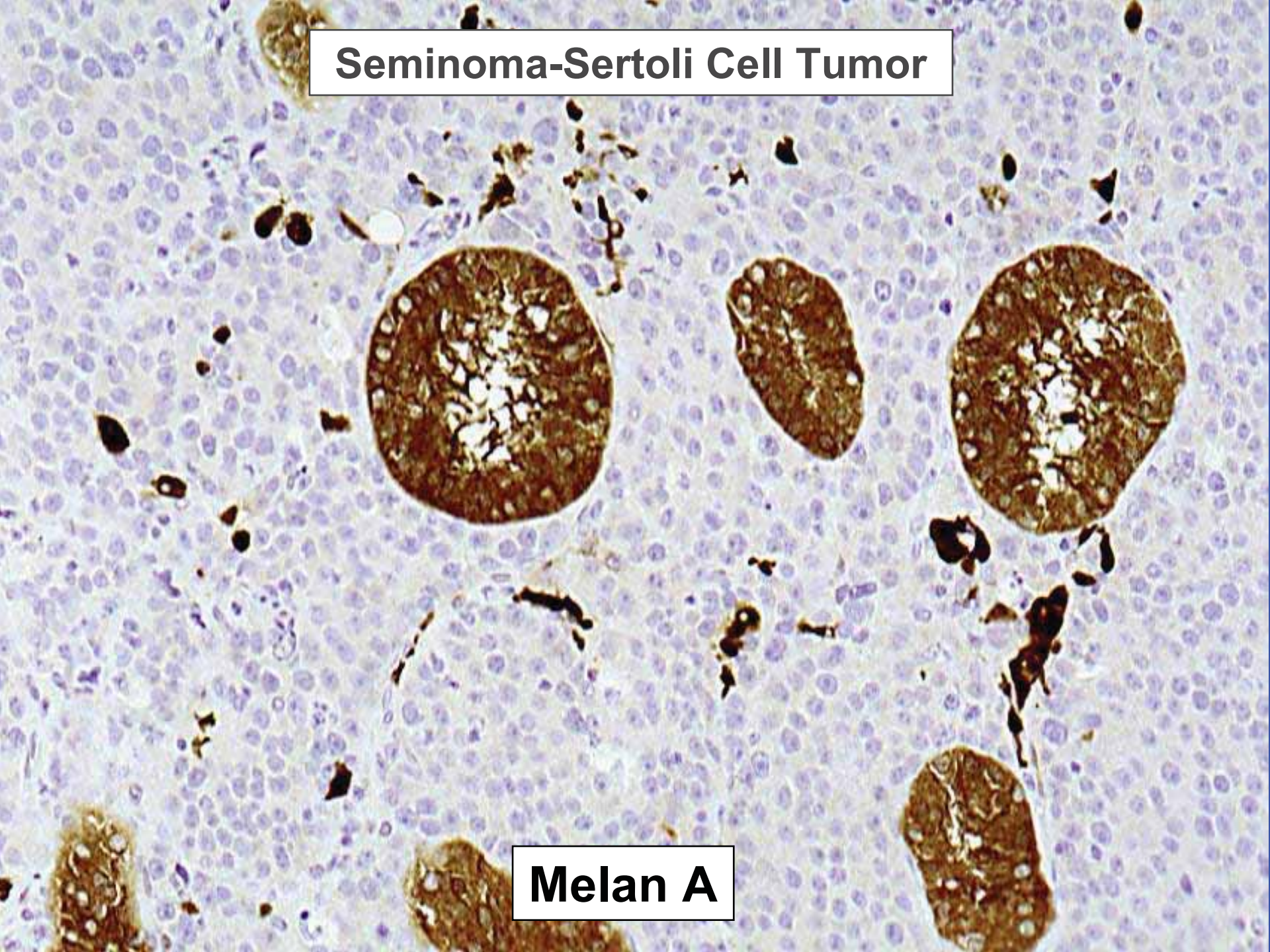
A photograph of a red wooden birdhouse mounted on a wooden post. The birdhouse is positioned in the upper left quadrant of the frame. The background consists of a lush green lawn and a dense line of trees. The lighting is bright, suggesting a sunny day. The overall scene is a typical outdoor setting.

**What's your
Diagnosis**

Malignant Granulosa Cell Tumor



Seminoma-Sertoli Cell Tumor



Melan A



Leydig Cell Tumor

This histological image shows a Leydig cell tumor. The tumor cells are arranged in cords and are characterized by their large, foamy cytoplasm and prominent nuclei. The brown pigment, identified as melanin, is a key diagnostic feature of this tumor type. The surrounding tissue consists of normal testicular cells, including Sertoli cells and germ cells, which are stained with hematoxylin and eosin (H&E).

Melan A

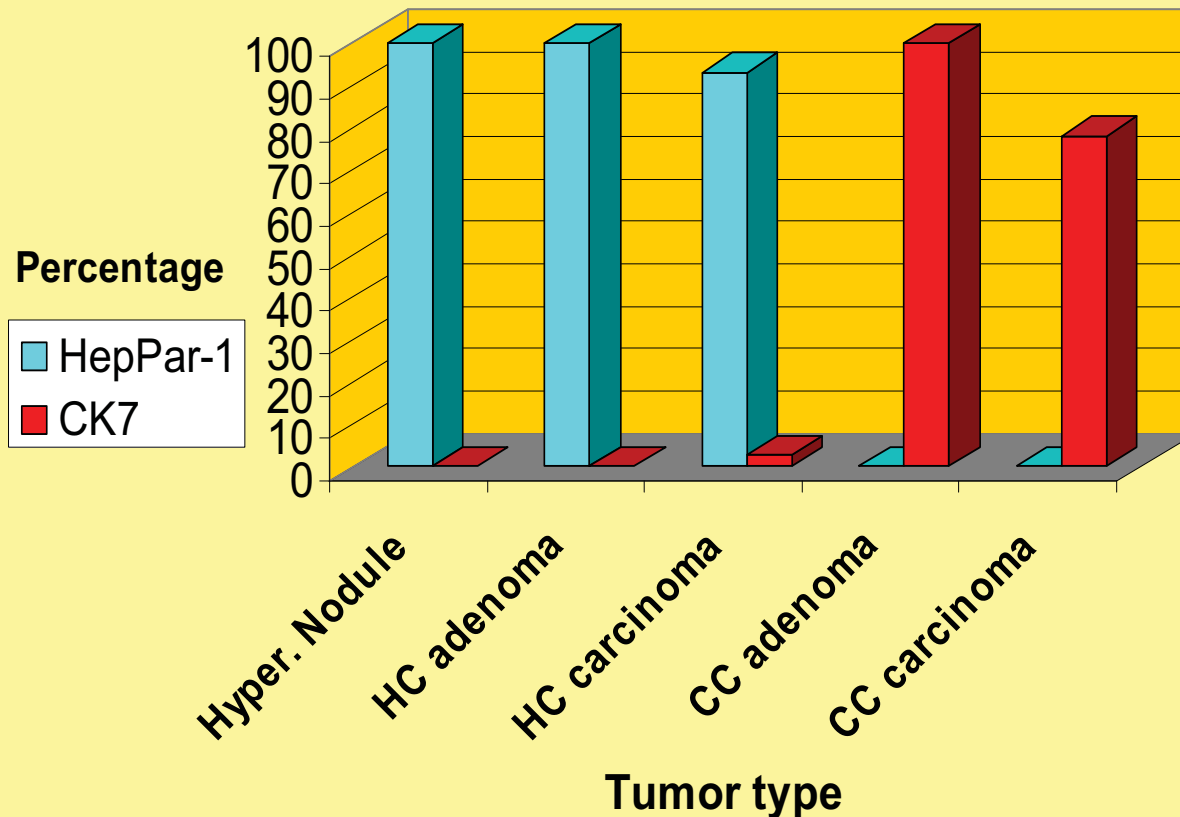
A high-magnification histological micrograph of a seminoma. The tissue is densely packed with large, uniform tumor cells. Each cell has a large, round, centrally located nucleus with a prominent, clear nucleolus. The cytoplasm is pale and contains some fine granules. The cells are arranged in a solid pattern with minimal stroma. Two white rectangular boxes with black borders are overlaid on the image. The top box contains the word "Seminoma" and the bottom box contains the text "Oct3/4".

Seminoma

Oct3/4

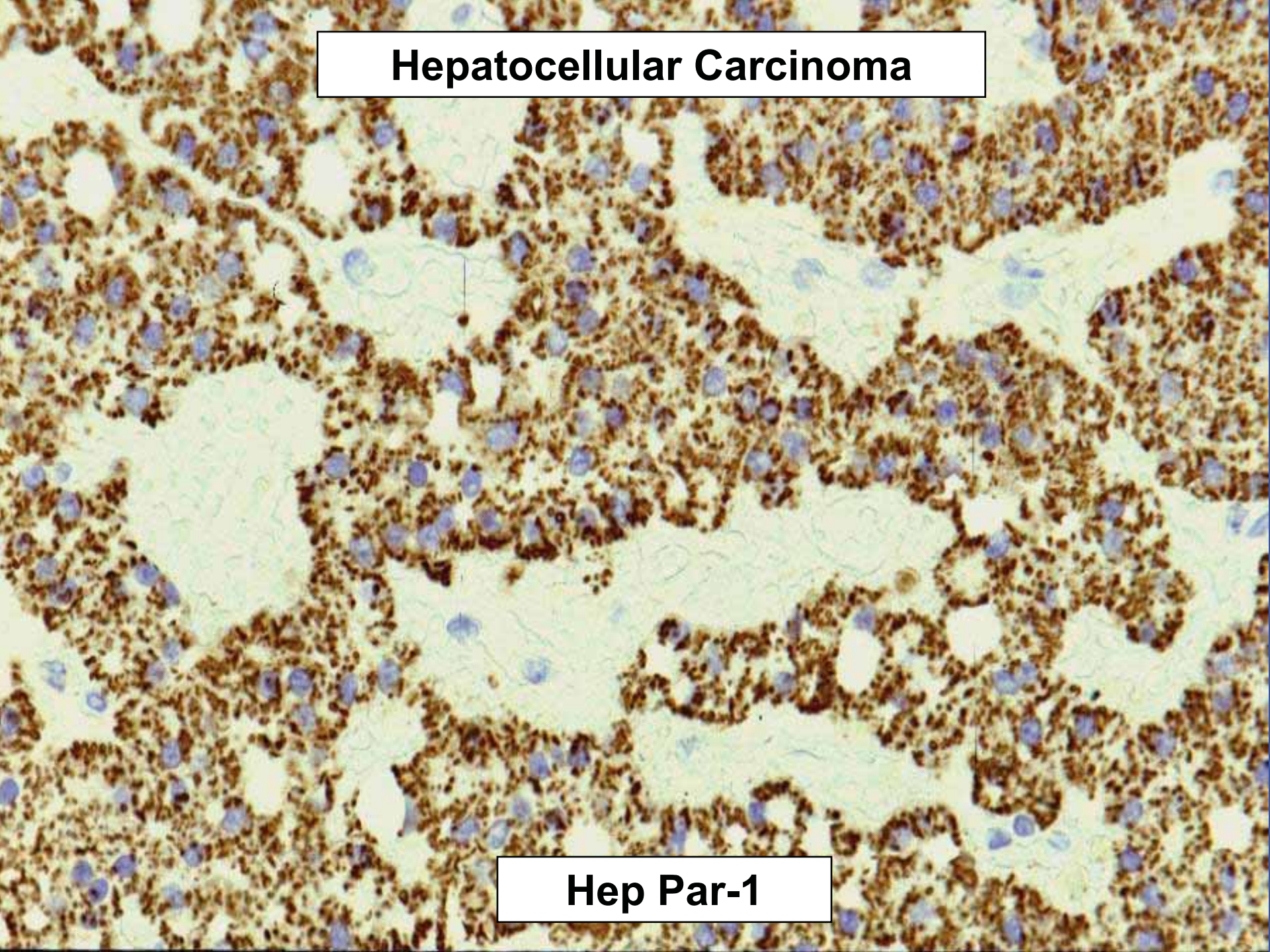
Canine Hepatic Tumors

HepPar-1 vs Cytokeratin 7



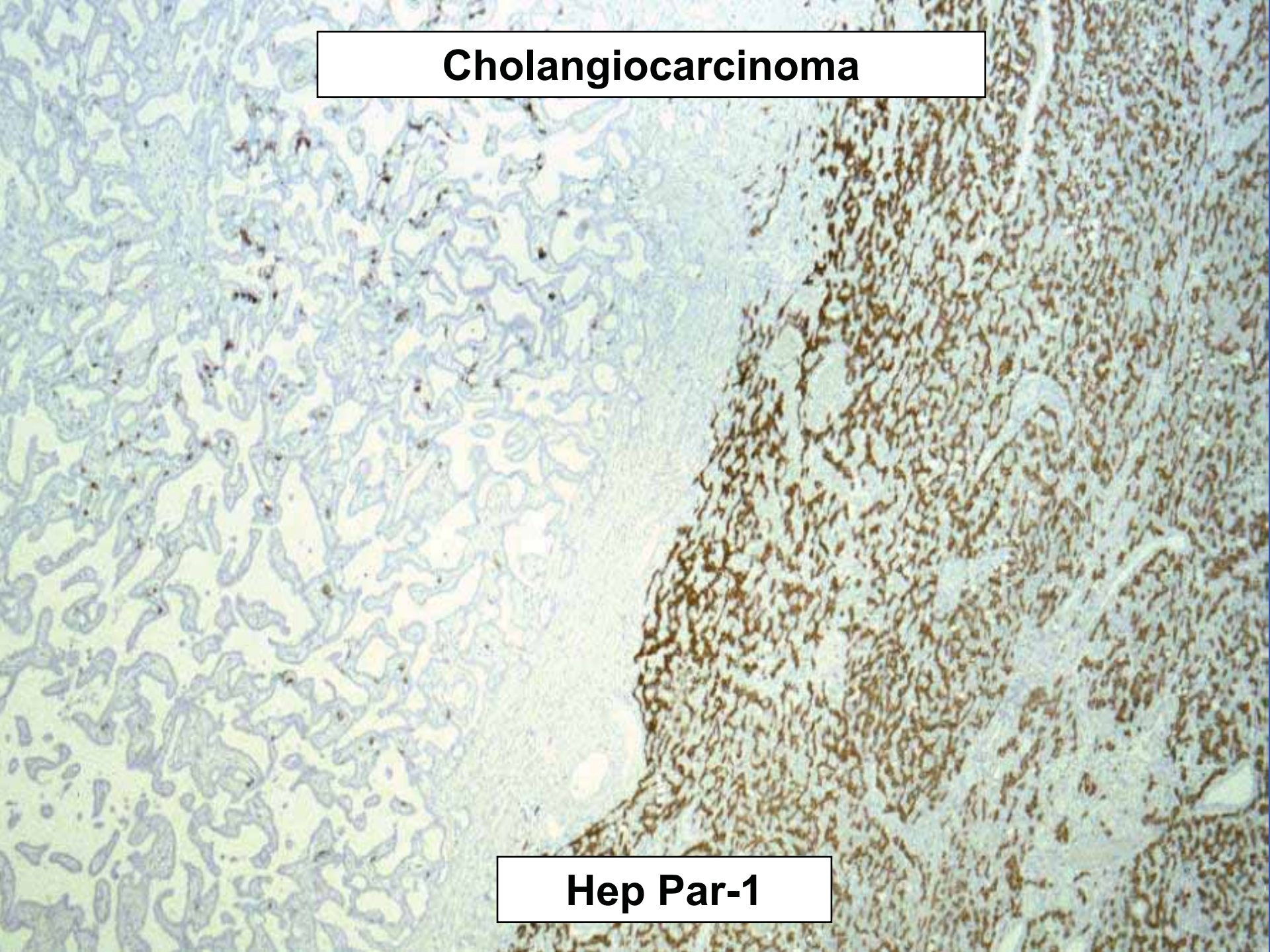
Hepatocellular Carcinoma

Hep Par-1

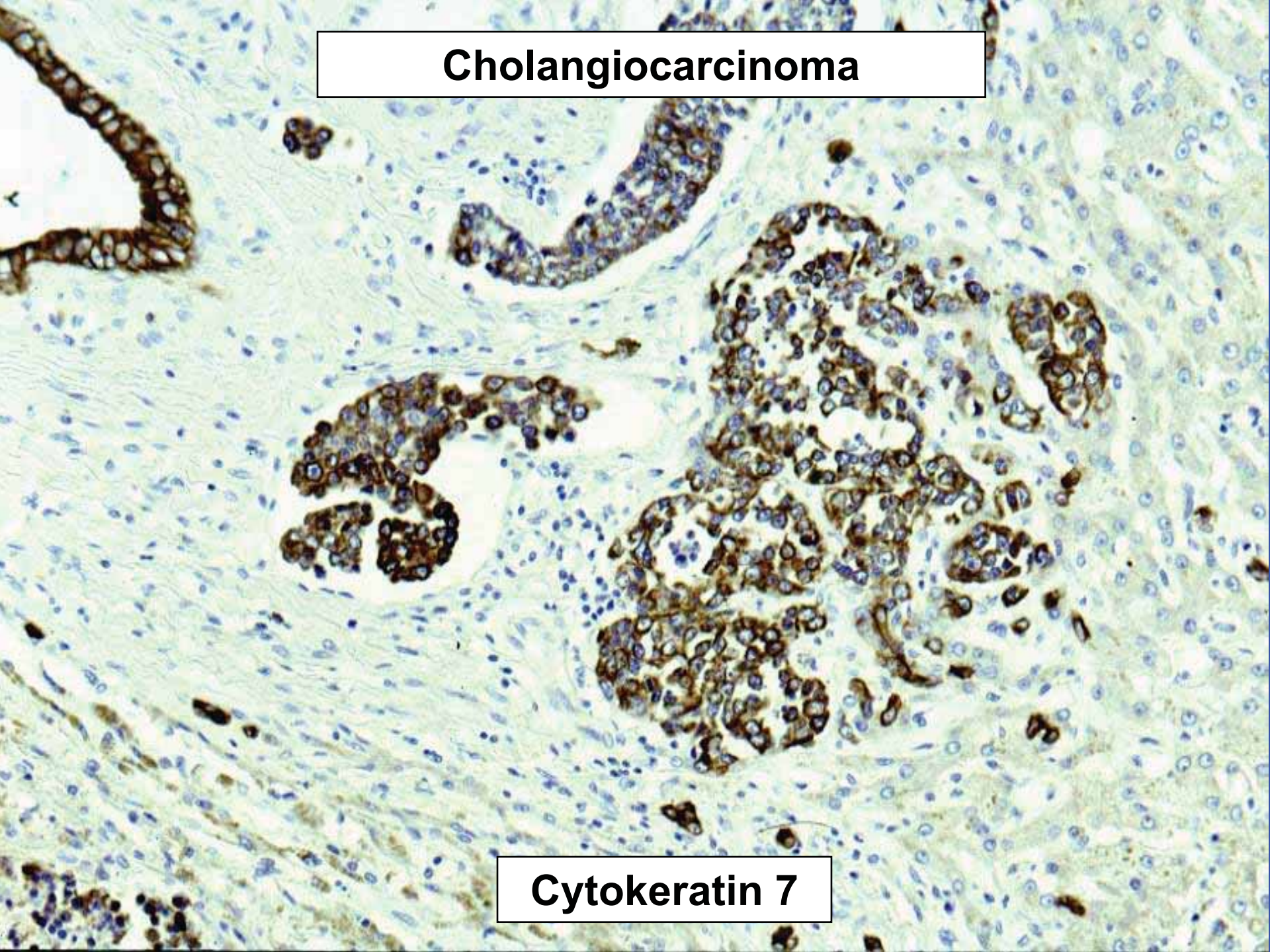


Cholangiocarcinoma

Hep Par-1

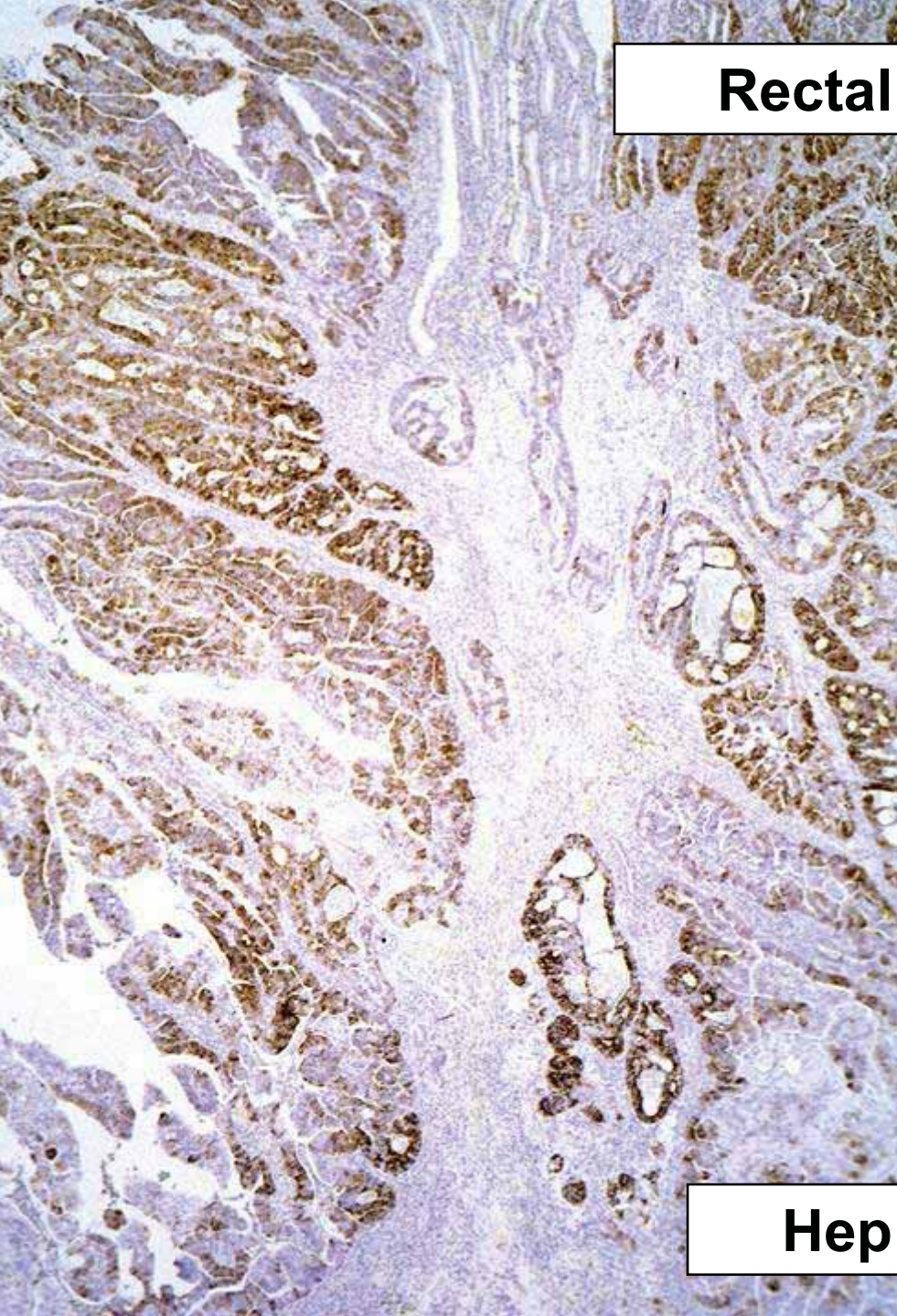


Cholangiocarcinoma

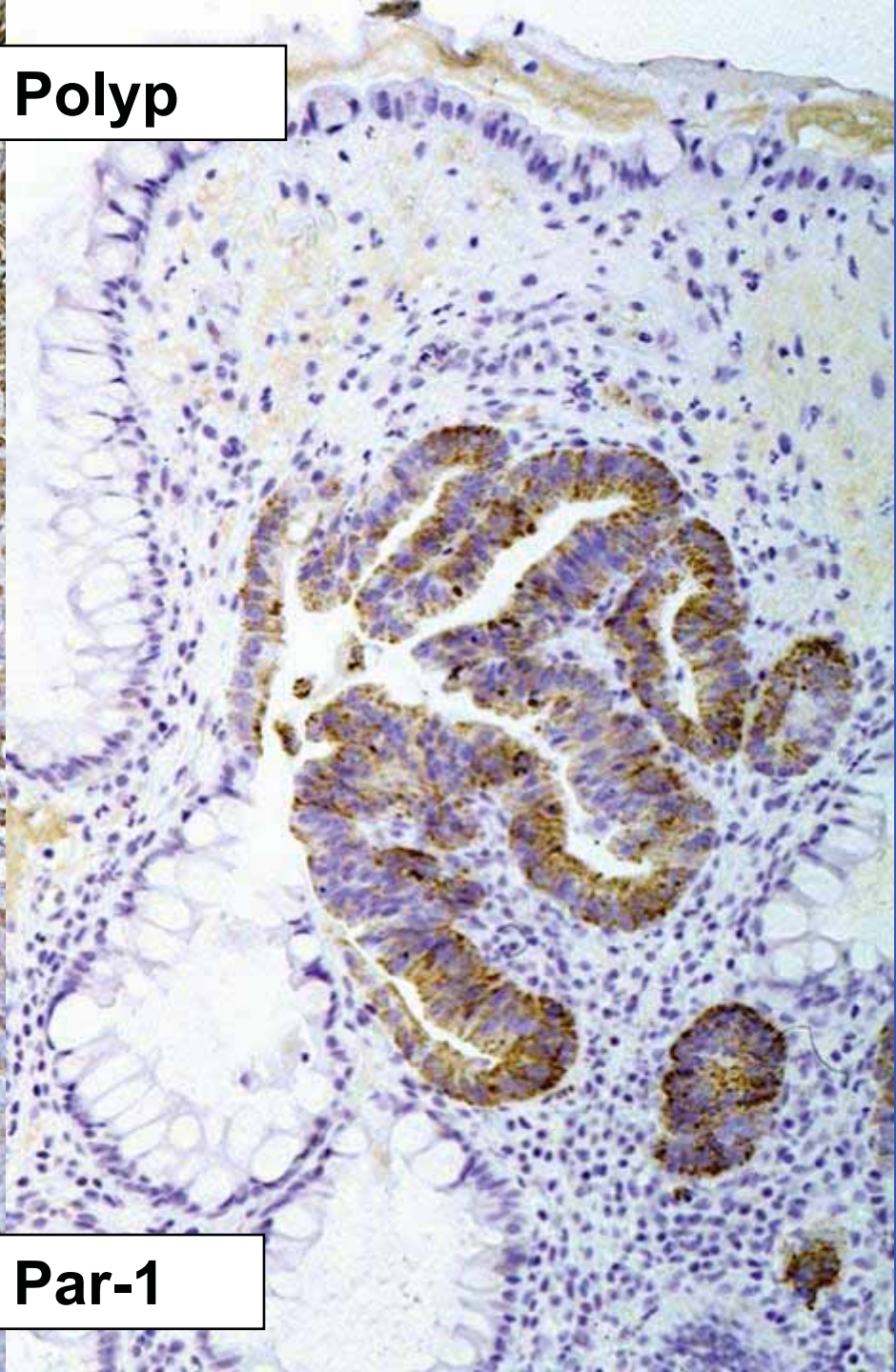


Cytokeratin 7

Rectal Polyp



Hep Par-1





We made it

Acknowledgement

Peter F. Moore



UC DAVIS

VETERINARY MEDICINE

Acknowledgement

Pepe Ramos-Vara



